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ABSTRACTS OF WORLD MEDICINE

It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 29 NO. 5 MAY, 1961

Pathology

EXPERIMENTAL PATHOLOGY

870. **Carcinogenic Studies on Petroleum Asphalt, Cooling Oil, and Coal Tar**
W. C. HUEPER and W. W. PAYNE. *Archives of Pathology* [*Arch. Path.*] **70**, 372–384, Sept., 1960. 7 figs., 45 refs.

In experiments at the National Institutes of Health, Bethesda, Maryland, various bituminous materials were tested for their carcinogenic properties. It was found that all of 4 road asphalts investigated produced tumours after skin painting or intramuscular injection in rats or mice. Fumes from heated coal tar and petroleum roofing asphalt on the other hand did not produce lung tumours in rats or guinea-pigs after inhalation for periods up to 2 years, but a condensate of the coal-tar fumes was highly carcinogenic to mouse skin and muscle tissues. A roofing asphalt was not carcinogenic when tested on mouse or rabbit skin. Paraffinic cooling-oil fog produced multifocal adenomatosis in the lungs of rats and guinea-pigs; only one squamous-celled carcinoma of the lung occurred—in a rat. This oil also produced a few skin and muscle tumours in mice following direct application. *G. Calcutt*

871. **Changes in the Lungs of White Rats after Intratracheal Injection of Coal and Peat Dust.** (Изменения в легких белых крыс при интратрахеальном введении им угольной и торфяной пыли)
M. A. KRAPOTKINA. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 39–43, Nov., 1960. 4 figs.

In order to obtain experimental evidence as to whether pneumoconiosis may be caused by coal dust white mice and rats were given intratracheal injections of peat and lignite dust in various doses on one or two occasions and the lungs thereafter examined histologically at intervals of one to 23 months. Evidence of pneumoconiosis was obtained. In its early stages this took the form of a diffuse interstitial fibrosis, more marked in the animals given peat dust. Later this was superseded by a focal reaction marked by the presence of nodules of dust cells. At periods of 12 months or more after exposure the lungs gradually became cleared of dust, which was then seen to accumulate in the regional lymph nodes. It is concluded that the inhalation of peat and lignite dust produces a mild pneumoconiosis which differs considerably from silicosis and is partially reversible in nature.
Basil Haigh

872. **Biological Properties of Vincaleukoblastine, an Alkaloid in *Vinca rosea* Linn., with Reference to Its Antitumor Action**
J. H. CUTTS, C. T. BEER, and R. L. NOBLE. *Cancer Research* [*Cancer Res.*] **20**, 1023–1031, Aug., 1960. 11 refs.

Vincaleukoblastine is a member of a new class of alkaloids containing both indole and dihydroindole moieties. It has a profound depressing action on bone marrow in rats, leading to severe granulocytopenia; megakaryocytes, however, are little affected. The drug appears to have little effect on other tissues such as the gut; it does not inhibit regeneration of the liver of the partially hepatectomized rat, and is less toxic to mice than to rats and guinea-pigs.

Tests carried out at the University of Western Ontario, London, Canada, in mice bearing transplantable leukaemias (L1210, P1534 and AKr) or Ehrlich ascites tumours showed that administration of the drug significantly prolonged survival times, the effectiveness of treatment depending on the amount and spacing of dosage and the time of institution of treatment after transplantation. Transplanted or spontaneous mammary tumours in C3H mice showed reduction in growth during treatment with vincaleukoblastine. Fischer rats bearing transplanted IRC741 leukaemia also responded favourably to treatment with the drug. *L. A. Elson*

873. **Antinuclear Factors in the Serum of Relatives of Patients with Systemic Lupus Erythematosus**
V. E. POLLAK, E. MANDEMA, and R. M. KARK. *Lancet* [*Lancet*] **2**, 1061–1063, Nov. 12, 1960. 2 figs., 13 refs.

In view of recent reports of the familial occurrence of systemic lupus erythematosus (S.L.E.) the authors examined sera from relatives of patients with this disease for the presence of antinuclear antibodies, using the fluorescein-labelled antibody technique.

When the serum dilution was 1:4 or higher positive results were obtained initially with serum from 45 out of 51 patients with S.L.E. At these dilutions sera from 40 healthy subjects were negative. The result of the test was therefore regarded as positive when antinuclear factors could be demonstrated in serum diluted 1:4 or more. On this basis positive results were obtained with 24 simple samples of serum from 50 relatives of 12 patients with S.L.E. The incidence of positive results was particularly high in female relatives (17 out of 26).

The gamma-globulin levels in the sera of these 50 relatives were estimated by the biuret method and paper

electrophoresis. Levels above the normal range (+2 S.D. of the mean for 62 healthy controls) were found in only 5 and levels below that range in 3.

M. Wilkinson

CHEMICAL PATHOLOGY

874. **The Effect of Test Feeds on the Plasma Lipids**
K. J. KINGSBURY, D. M. MORGAN, and P. C. SHERVINGTON. *Lancet* [*Lancet*] **2**, 1045–1049, Nov. 12, 1960. 4 figs., 25 refs.

The authors of this paper from St. Mary's Hospital, London, describe a quick and reproducible biological test for the definition and identification of the dietary factors influencing human lipid metabolism. They point out that the test is not offered as an alternative to long-term experiments, but as a supplementary method especially useful for rapid biological assays.

The subjects were not allowed any dietary fat intake during the 12 hours preceding the experiment, but were permitted a light breakfast consisting of dry toast, marmalade, and fat-free drinks 2 to 3 hours before. They were given 50 g. of oil emulsified with 50 ml. of skimmed milk and 50 to 100 ml. of tap-water as a single feed, followed (to avoid nausea which might delay the absorption) by a strong-tasting drink, such as blackcurrant cordial. Samples of blood were taken before the feeds and at 1½, 3½, 5½, 7 to 9, and 24 hours afterwards. Determination of the different lipid fractions showed that the lipid response, especially the plasma cholesterol and plasma phospholipid changes, could be reproduced in different subjects or in the same subjects after long intervals. Advantages of the method are the small amount of material needed, the speed with which it can be performed, and the ease of experimental control.

Z. A. Leitner

875. **Serum Protein Paper Electrophoresis in Patients with Cystic Fibrosis**
M. N. GREEN, L. L. KULCZYCKI, and H. SHWACHMAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 365–372, Sept., 1960. 19 refs.

At the Children's Medical Center, Boston, the total serum protein content was determined and the electrophoretic pattern of the serum proteins studied in 114 cases of cystic fibrosis. The degree of deviation from the normal pattern was assessed and was compared with the clinical condition of the patient, which was evaluated by means of a rating system in which the patient's general activity, physical condition, and nutritional status and the radiological findings in the chest were all given equal weight. A score of less than 40 out of a possible total of 100 points was regarded as indicating severe disease.

The results are shown in tabular form, the patients being grouped first according to age and then according to clinical rating. There was a slight diminution in the average total serum protein content in 12 infants less than one year old, but in the other age groups the level was relatively normal. As the disease progressed marked changes in the electrophoretic pattern took place. A reduction in the serum albumin concentration and an increase in that of γ globulin were noted, the degree of change being closely correlated with the severity of the disease, while there was a significant, but slighter, increase in the α_2-globulin concentration. There was also a progressive increase in the γ-globulin concentration with age. No significant changes in the serum levels of α_1 globulin or β globulin were observed at any stage of the disease.

The changes in the serum protein pattern observed were those to be expected in the presence of liver disease, chronic pulmonary infection, and malnutrition. It was not possible to separate the effects of these causes on the composition of the serum proteins.

W. H. Horner Andrews

HAEMATOLOGY

876. **Changes in the Blood Prothrombin Level in Infants with Pneumonia in the First Year of Life.** (Уровень протромбина крови и его колебания при пневмонии у детей первого года жизни)
N. I. PODVORČANNAJA. *Педиатрия* [*Pediatrija*] **38**, 32–36, Nov., 1960. 19 refs.

The author has investigated the blood prothrombin content in 75 children with pneumonia. All the patients were in the first year of life and the majority were receiving artificial or mixed feeding. In many cases the liver was enlarged during the acute phase of pneumonia, this enlargement receding during convalescence, and the blood clotting time was prolonged.

The failure of blood clotting is considered to have resulted from a dysfunction of the synthesis of prothrombin in the liver. The prothrombin time depends on the concentration of prothrombin in the blood. This study has shown that in normally nourished children suffering from pneumonia of marked or medium severity there is in the acute phase of the illness a definite diminution in the prothrombin content of the blood, amounting in 8 out of 14 cases to 89% and in 2 to 76%. It was also demonstrated that the greater the enlargement of the liver during the illness, the greater the degree of dysfunction of prothrombin formation. It is pointed out that the clinical recovery of the child does not always coincide with complete recovery of hepatic function.

H. W. Swann

877. **Technical Errors in the Blood Sedimentation Rate Estimation**
D. M. LEWSEY and J. M. SIMPSON. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **109**, 160–168, 1960. 4 figs., 7 refs.

An investigation was carried out at Guy's Hospital, London, to assess the extent to which errors arose in the estimation of erythrocyte sedimentation rates. Such estimations are made as a routine by Westergren's method on the medical wards. The most important cause of error was the fact that the tubes were often not properly vertical because the stands were warped; errors of up to 300% could occur in this way. Other important sources of error were inaccurate measuring of citrate dilutions and failure to dry the tubes properly

before filling. Variations in ward temperature and draughts were found not to be very important. A technique designed to eliminate such errors is described.
M. C. G. Israëls

878. **Effect of Phenindione and Bed Rest on Blood Coagulability following a High-fat Intake**
G. A. McDonald and H. W. Fullerton. *Lancet* [*Lancet*] **2**, 1111–1112, Nov. 19, 1960. 4 refs.

The authors, from the University of Aberdeen, describe experiments showing the effect of phenindione therapy and bed rest on the coagulability of the blood following a high fat intake, using the recalcified plasma clotting (R.P.C.) time as a reliable measure of *in-vitro* coagulability. They show that the shortening of the R.P.C. time normally found after a high-fat meal is significantly less in ambulant subjects than in those confined to bed, and that this shortening is abolished in both groups by administration of phenindione. Estimations of the degree of lipaemia at the time of estimation of the R.P.C. time showed that this is less in ambulant than in resting subjects, but that the action of phenindione is not due to its effect in reducing lipaemia.

It is tentatively suggested that the beneficial effect of phenindione therapy in myocardial infarction may be due in part to its effect in reducing coagulability after high-fat meals. Nothing can be gained by lowering the fat intake of patients with myocardial infarction to reduce coagulability *in vivo* provided they are being treated with phenindione. *A. Brown*

879. **Evaluation of Thrombotest in the Control of Anticoagulant Therapy**
H. Lempert and L. Poller. *Lancet* [*Lancet*] **2**, 1115–1119, Nov. 19, 1960. 4 figs., 27 refs.

The value of the " thrombotest " method for the control of anticoagulant therapy was compared with that of Quick's one-stage prothrombin-time test and that of the prothrombin and proconvertin (P.P.) test of Owren and Aas in 43 patients at Manchester Royal Infirmary receiving phenindione. The patients were divided into two groups. Group A (31 patients) were tested on a total of 415 occasions over a period of 530 days. When anticoagulant therapy in these patients was controlled by Quick's method about 30% of the simultaneous thrombotest results were below the therapeutic range, suggesting that too much anticoagulant had been given. Group B (12 patients) underwent a total of 154 tests over 246 days. When treatment in this group was controlled by the thrombotest method about 30% of the simultaneous Quick-test results were above the therapeutic range, suggesting that too little anticoagulant had been given. Haemorrhage occurred in 4 cases, in 3 of which the results with the P.P. test and the thrombotest were below the therapeutic level of 10%, while the Quick test showed the prothrombin activity to be in the therapeutic range—that is, above 15%.

The chief advantage of the thrombotest is that its results are as reliable as those of the more complicated P.P. test. Its disadvantages compared with the Quick prothrombin-time test include the greater care necessary in collecting blood specimens and the difficulty of siliconing glassware and syringes and of reconstituting the freeze-dried reagent, this last being expensive.

The authors consider that before the Quick test is replaced by the thrombotest for the routine control of anticoagulant therapy more experience is required. " Meanwhile it is suggested that safer control will be obtained if the Quick prothrombin time, using acetone-dried brain extract, is kept at not more than twice normal, and the thrombotest at not more than 3 to 3½ times normal. No one-stage method is entirely safe in controlling anticoagulant treatment." *H. Caplan*

880. **Anti-hemophilic Globulin Levels in Carriers of Hemophilia A**
S. I. Rapaport, M. J. Patch, and F. J. Moore. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 1619–1625, Nov., 1960. 5 figs., 11 refs.

The authors report from the University of Southern California, Los Angeles, the results of assays of the plasma anti-haemophilic globulin (A.H.G.) level in 35 " obligatory " carriers of haemophilia A (that is, mothers or daughters of haemophiliacs) and 30 normal women, using the Pool–Robinson assay technique, the results being compared with those in a standard reference plasma taken from a male subject at 2-week intervals. Storing the plasma at −20° C. was shown to prevent a fall in the A.H.G. level. The estimations were carried out either on duplicate samples of plasma withdrawn on each of 2 successive days or on a single sample taken weekly in 4 successive weeks. By the methods of variance analysis it was shown that differences in A.H.G. levels between individuals far exceeded, as expected, those within or between days for the same individual, and that the variations between days were significantly greater than differences within days and were of the same order of magnitude as those between weeks. Single estimations on a number of successive days thus increase the accuracy of the result more than do duplicate estimations made on the same day. The menstrual cycle and the age of the patient did not affect the A.H.G. level.

In the normal women the mean A.H.G. level was 92% of the reference plasma, whereas in the carriers the mean was 58%. The range, however, was wide in both groups (52 to 133% in the normal subjects and 22 to 135% in the carriers), indicating that many factors influence the A.H.G. level apart from the single haemophilia gene. One carrier, whose A.H.G. level was 22% of normal, experienced clinically significant bleeding; it is suggested on the basis of the distribution of A.H.G. levels in the present series that A.H.G. values low enough to cause significant bleeding, that is, below 30%, occur in about 20 carriers per 1,000. Calculations of probability indicate that estimation of the A.H.G. level will detect with reasonable accuracy (four chances in five) about 75% of true carriers of haemophilia A in a population of potential carriers (that is, daughters of mothers who are carriers) and about 66% of the normal members in a potential carrier population. However, a potential carrier even with a very high A.H.G. level still runs a one-in-five risk of being a true carrier. *A. Brown*

MORBID ANATOMY AND CYTOLOGY

881. **Histological Changes in the Duodenal Mucosa in Coeliac Disease. Reversibility during Treatment with a Wheat Gluten Free Diet**
C. M. ANDERSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **35**, 419–427, Oct., 1960. 14 figs., 18 refs.

The histological changes in the duodenal mucosa in coeliac disease were studied in biopsy specimens obtained from 17 children (aged 14 months to 10 years) at the Royal Children's Hospital, Melbourne, in whom the disease or wheat-gluten intolerance had recently been diagnosed. All the children were subsequently treated by excluding wheat gluten from the diet. In 11 of the cases biopsy specimens were taken at intervals during treatment.

The histological changes were of a consistent pattern but varied in severity. The chief characteristic was the straight, flat edge of the mucosal surface. The epithelial cells became flattened and the number of goblet cells on the surface was reduced. In biopsy specimens obtained from 11 children who were followed up during their first year of treatment with a diet free from wheat gluten these changes had completely or partially disappeared. The author states that reduction in surface area exposed to digested foodstuffs is believed to be responsible for malabsorption; in the present series, however, there was no correlation between the severity of the lesion and the degree of malabsorption as determined by fat balance studies. It is also characteristic of coeliac disease that symptoms may not be as severe in late childhood as in early life, in spite of an apparently greater absorption defect.

Present theories concerning the toxic mechanism of wheat gluten are briefly discussed, but no new evidence is offered to account for it. *A. W. H. Foxell*

882. **Unique Morphologic Features of Whipple's Disease: a Study by Light and Electron Microscopy**
W. S. HAUBRICH, J. H. L. WATSON, and J. C. SIERACKI. *Gastroenterology* [*Gastroenterology*] **39**, 454–468, Oct., 1960. 7 figs., 29 refs.

The systemic nature of Whipple's disease is confirmed by this report of the findings by light and electron microscopy in 21 cases studied at the Henry Ford Hospital, Detroit, Michigan. Distinctive cells containing a diastase-resistant, periodic-acid–Schiff (P.A.S.)-positive substance, called by Sieracki (*A.M.A. Arch. Path.*, 1958, **66**, 464) "sickle-form-particle-containing cells," were demonstrable in the gastro-intestinal tract and lymph nodes especially, but also in liver, pancreas, spleen, lymph nodes, bone marrow, cardiovascular system, lungs and pleura, adrenals, and central nervous system. Imprints of intestinal mucosal biopsies in 2 patients and of peripheral lymph nodes in 3 patients were of considerable diagnostic value in revealing the cells. When examined by the electron microscope these cells had a distinct ultra-structure; their cytoplasm contained both clusters of vacuolated bodies 0·05 to 0·1 μ in diameter and sheets and nests of cylindrical particles 0·10 to 0·15 μ in diameter and 0·8 to 1·7 μ in length; the latter were also found free in the tissue spaces. It is suggested that the P.A.S.-positive particles constitute a phase in the elaboration of an abnormal protein–carbohydrate complex by mutant reticular cells. *A. Wynn Williams*

883. **Paneth Cells in the Large Intestine in Ulcerative Colitis**
A. J. WATSON and A. D. ROY. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **80**, 309–316, Oct., 1960. 6 figs., 29 refs.

In man Paneth cells have been reported to be almost completely confined to the fundi of the crypts of the mucosa of the small intestine, though a few may also be found irregularly in the mucosa of the caecum and appendix. The authors, working at the Western Infirmary, Glasgow, have examined 5 specimens of the entire adult intestine obtained at necropsy and 7 biopsy specimens of colon obtained at operation from patients without intestinal disease. In addition they have examined surgical, biopsy, and necropsy specimens of the colon and rectum from 23 cases of ulcerative colitis and 59 cases of other diseases of the large intestine, including 30 cases of carcinoma, 10 of simple epithelial tumours, 10 of diverticulitis, and 5 of post-irradiation proctitis. The material was stained with haematoxylin and eosin and Masson's trichrome stain.

The above distribution of Paneth cells was confirmed in the normal subjects. Paneth cells were found to occur regularly in the mucosal crypts of the large intestine in cases of ulcerative colitis, especially in the ascending, transverse, and descending colon; they were less common in the sigmoid colon and occurred only exceptionally in the rectum. No other condition of the large intestine was found to be so constantly associated with the presence of Paneth cells in the mucosa. The possible significance of this finding is discussed briefly. *R. Wyburn-Mason*

884. **Thromboembolic Pulmonary Arterial Necrosis and Arteritis in Man: a Study of Eleven Autopsied Cases**
J. S. MEYER. *Archives of Pathology* [*Arch. Path.*] **70**, 445–454, Oct., 1960. 8 figs., 20 refs.

A chance observation led the author, at Washington University School of Medicine, to examine 23 cases of pulmonary thromboembolism for the presence of necrosis in the walls of large pulmonary arteries. Foci of necrosis were found in 11 out of the 23 cases studied; only one of the patients was under the age of 40. The lesions were seen only in segments of artery occupied by occlusive thrombi, the thrombi being either unorganized or showing early peripheral organization. In no case was there intrapulmonary disease which could have fully accounted for the thrombosis. The inflammatory lesion related to the necrotic lesion was in no sense specific, and was non-granulomatous in type. In discussing the aetiology full consideration is given to experimental pulmonary embolism. The author suggests that, in addition to obstruction of the blood supply, the constant tension on the vascular wall exerted by the impacted embolus may be important. As the inner part of the

media obtains its metabolites from the lumen of the vessel this mechanism would be upset, thus resulting in further injury to an already damaged wall.

G. J. Cunningham

885. **The Role of Smooth Muscle Cells in the Fibrogenesis of Arteriosclerosis**

M. D. HAUST, R. H. MORE, and H. Z. MOVAT. *American Journal of Pathology* [*Amer. J. Path.*] **37**, 377–389, Oct., 1960. 18 figs., 31 refs.

The authors report, from Queen's University and the Kingston General Hospital, Ontario, Canada, investigations into the nature of cells concerned with the avascular organization of the "insudate" of blood proteins into the intima and of mural thrombi occurring in the repair phase of many arteriosclerotic lesions.

Morphologically and histochemically, these cells appear identical to known smooth-muscle cells and entirely different from known fibroblasts. The shape of the cell and the nucleus with its coarse chromatin distribution, the eosinophilia of the cytoplasm, the presence of numerous fibrils which are parallel to the longitudinal axis and extend out of the cytoplasm into the connective tissue, the intense eosinophilia of these fibrils and their affinity for phosphotungstic acid haematoxylin, the contractility of the cell which leads to a characteristically shaped nucleus, and the close association of the cells with elastic fibres coating it are all features identical to those of control smooth-muscle cells in the uterus and intestine. On the other hand the corresponding features are altogether different from those of fibroblasts. [These observations are illustrated in a series of excellent photomicrographs.]

The origin of smooth-muscle cells in areas of avascular granulation tissue in arteriosclerosis is uncertain; the authors consider that they are derived from regenerating endothelium.

H. Caplan

886. **Relationship of Aschoff Bodies in Cardiac Atrial Appendages to the Natural History of Rheumatic Heart Disease**

F. G. DALLDORF and G. E. MURPHY. *American Journal of Pathology* [*Amer. J. Path.*] **37**, 507–519, Nov., 1960. 7 figs., 35 refs.

The authors have investigated the relationship between the preoperative clinical course and the occurrence of Aschoff bodies in the left auricular appendage removed at commissurotomy in patients with rheumatic heart disease.

The study covered records of 81 patients (64 women and 17 men aged 20 to 40) collected from the files of the New York Hospital. Histologically, the cases were divided into 2 groups according to whether Aschoff bodies were or were not present. [In the description of Aschoff bodies as seen in this material the authors categorically state that these bodies originate from "rheumatic injury to heart muscle", either striated or smooth, mostly in or just beneath the subendocardium. Such an origin is by no means generally agreed; for a recent critical discussion see Ehrlich (*Ann. N.Y. Acad. Sci.*, 1960, **86**, 1006).] Clinical division was into 3 groups: Group 1 showed steady progression of cardiac symptoms for 18 months or less before operation; Group 2 showed similar deterioration but for a longer period; Group 3 had severe rheumatic heart disease, but without deterioration for the last 2 years. Groups 1 and 2 were each subdivided into (A) those with definite progression of symptoms, and (B) those with only minimal and indefinite progression.

Of the total of 81 cases, 50 are reported to have had Aschoff bodies. In clinical Group 3, 5 out of 13 patients showed such bodies, while in Subgroup 1A positive results were obtained in 19 out of 20 and in Subgroup 2A in 13 of 17 patients. Thus a relationship appears to have been established between the clinical course and the incidence of Aschoff bodies in rheumatic heart disease.

G. Loewi

887. **Significance of Megakaryocytes in the Search for Tumor Cells in the Peripheral Blood**

J. W. RAKER, P. D. TAFT, and E. E. EDMONDS. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 993–996, Nov. 17, 1960. 4 figs., 15 refs.

At Massachusetts General Hospital, Boston, the authors examined for tumour cells 222 samples of blood from 144 patients, all but 9 of whom had a malignant tumour. The blood was taken from a peripheral vein or from a vein draining the tumour-bearing area. The technique involved destroying erythrocytes and granulocytes by treatment with streptolysin, passing through a "millipore" filter, and staining the filtrate directly by a Papanicolaou technique (Malmgren *et al.*, *J. nat. Cancer Inst.*, 1958, **20**, 1203).

Repeatedly, large cells with lobulated nuclei were found. The nuclei measured 14 to 21 μ in greatest diameter and there were no apparent nucleoli; the cytoplasm measured up to 33 μ, was granular, and had sharp borders in some cells but was ill-defined or absent in others. These cells, which were found in 60 patients (42%) were, at the beginning of the study, considered to be tumour cells. Further experience suggested that they were possibly megakaryocytes, and exactly similar cells were found in the blood of 2 patients suffering from polycythaemia.

The authors emphasize that megakaryocytes occur in circulating blood and can be confusing to the searcher for tumour cells. In this series only 2 patients were found with definite positive samples; one had reticulosarcoma, the other carcinoma of the breast. In both cases the cells found in the blood resembled those of the primary tumour in size and shape.

H. Caplan

888. **The Differential Diagnosis of Tumour Cells in Circulating Blood**

R. F. ALEXANDER and A. I. SPRIGGS. *Journal of Clinical Pathology* [*J. clin. Path.*] **13**, 414–424, Sept., 1960. 25 figs., 25 refs.

The finding of circulating tumour cells has been reported from various centres in recent years, the incidence in cases of malignant disease ranging from 16 to 59%. In this paper from the Churchill Hospital, Headington, Oxford, the authors draw attention to the

pitfalls in diagnosing tumour cells in the blood. They point out the disadvantage of using stains not generally used in haematology—they themselves use the May–Grünwald–Giemsa staining method—and illustrate many types of non-malignant cell which may have been misdiagnosed as tumour cells in the past.

The present study was carried out on leucocyte concentrates prepared by a dextran-sedimentation technique from the blood of 140 patients with known malignant disease and 60 control subjects. A special effort was made to include patients with extramedullary haematopoiesis, leuco-erythroblastic anaemia, and terminal illnesses in whose blood some of the lesser-known non-malignant cells might be expected to occur. Most of the samples were taken from the antecubital vein, but 45 samples were taken at operation from veins draining malignant tumours or other (" control ") lesions. The stained slides were searched for unusual cells, several million leucocytes being scanned in each case.

In the whole series, excluding cases of leukaemia, myeloma, and reticulosarcoma, " acceptable " tumour cells were found in the blood of only 7 patients (3 with carcinoma of the bronchus and one each with carcinoma of the breast, carcinoma of the stomach, malignant melanoma, and malignant synovioma); all these patients died within 5 months of the finding of circulating tumour cells. No malignant cells were found in the blood of patients with operable carcinoma, even in samples of blood from the venous drainage of the tumour.

The authors suggest that much of the confusion in diagnosis is due to the presence of unusual but non-malignant cells in the blood of patients with malignant disease. For example, carcinomatosis involving the skeleton may produce a leuco-erythroblastic reaction, and the numbers of plasma cells and their precursors are also often increased in malignant disease. It is therefore stressed that later histological confirmation that malignant disease was present does not constitute sufficient proof that a " positive " cytological finding was correct. Indeed, " the identification of a malignant cell on morphological grounds is only an opinion and cannot be verified ". They conclude that " there is still room for further research into the non-malignant cells occurring in the circulation before statistical data on the frequency of circulating tumour cells can be considered accurate".

I. Berkinshaw-Smith

889. **Air-flow as an Etiologic Factor in Metaplasia in the Tracheobronchial Tree**

A. C. HILDING. *Archives of Pathology* [*Arch. Path.*] **70**, 550–561, Nov., 1960. 6 figs., 18 refs.

Squamous metaplasia in the nose can be related to air flow, and bronchial cancer may conceivably have its origin in foci of squamous or other types of metaplasia. It was therefore decided to investigate the possibility of metaplasia in the lower respiratory tract being related to air inflow. In a histological study at St. Luke's Hospital, Duluth, Minnesota, on suitable necropsy material from 55 patients varying in age from 15 to 94 years a comparison was made of areas subject to the impact of air flow (medial wall of left main bronchus) and of those where no obstruction occurred (medial wall of right main bronchus). No evidence could be found to support the hypothesis that air flow was a factor causing metaplasia.

G. J. Cunningham

890. **Nerve Fibre Degeneration in the Brain in Amyotrophic Lateral Sclerosis**

M. C. SMITH. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 269–282, Nov., 1960. 18 figs., 17 refs.

The usual concept of amyotrophic lateral sclerosis is of a degenerative condition of the lower motor neurones of the spinal cord and cranial nerves and of the upper motor neurones in the hemispheres. In the cord the typical picture is one of degeneration of the cortico-spinal fibres and sometimes also of the spino-cerebellar and other anterior and lateral column fibres. Cases have been described in which degeneration extended throughout the cortico-spinal system, but it is more frequently stated that degeneration does not extend rostrally farther than the medulla or pons. Some degeneration has been reported in other parts of the brain.

In this paper from the National Hospital, Queen Square, London, the author reports the results of a study of the distribution of the degeneration in the central nervous system in 7 cases of the disease. Blocks of tissue from the brain and spinal cord were stained with thionin, haematoxylin, and by the van Gieson, Loyez, Marchi, and Weigert–Pal staining methods. She describes and illustrates the findings in some detail [for which those interested should consult the original paper]. Degenerating myelinated nerve fibres were shown to be present from the cortex throughout the brain-stem and the cord in every case. They were distributed widely in the cortex, being found not only in the pre-central and para-central lobules, but also abundantly in the post-central gyrus and adjacent parietal and frontal gyri and elsewhere. The majority appeared to pass into the region ascribed to the cortico-spinal system in the brain-stem and continued into the cord. Similar degenerating fibres were found in the corpus callosum; they also passed between the main group of degenerating fibres in the internal capsule and the lateral nucleus of the thalamus, and were present in the basal ganglia (notably the ansa lenticularis and fasciculus lenticularis) and in the substantia nigra, tegmentum, and reticular formation of the brain-stem. In the discussion it is suggested that in view of the distribution of degenerated fibres here demonstrated " it is most probable that many arise in the globus pallidus . . . If this is indeed so, the involvement of the globus pallidus may contribute to the severity of the muscle paralysis in amyotrophic lateral sclerosis".

R. Wyburn-Mason

891. **The Finding of Chronic Pyelonephritis in Males and Females at Autopsy**

S. E. T. KLEEMAN and L. R. FREEDMAN. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 988–992, Nov. 17, 1960. 29 refs.

The authors, in an attempt to establish the aetiological relationship between clinical urinary-tract infection and the necropsy finding of chronic pyelonephritis, have reviewed 1,526 consecutive necropsies performed at the

Grace–New Haven Community Hospital, New Haven, Connecticut, from January, 1957, to January, 1959. Among this material there were 97 cases of chronic pyelonephritis and 5 cases of pyelitis, comprising 6·7% of the total series; 65 of the 102 patients were males and 37 females. Of these patients there were 49 (40 males and 9 females) with obstruction or other primary abnormality of the genito-urinary tract and 53 (25 males and 28 females) in whom such lesions were not demonstrable. There were also 66 patients (39 males and 27 females) with scarred kidneys. The exclusion of cases with obstructive lesions from this group left 19 cases (9 in males and 10 in females). In both groups the histological changes and the incidence of hypertension were similar in the two sexes.

It appears, then, that there is a discrepancy between the approximately equal sex distribution of chronic pyelonephritis in the absence of obstruction at necropsy and the 10:1 female preponderance of urinary-tract infection in the absence of obstruction in life (Freedman, *International Symposium on the Biology of Pyelonephritis*, Henry Ford Hospital, Detroit, Michigan, 1959). This discrepancy supports the hypothesis that histological changes similar to those of chronic pyelonephritis may result from diseases other than bacterial infection of the kidney. The present authors list old age, sterile hydronephrosis, potassium deficiency, drug ingestion (phenacetin or sulphonamide), immunological reactions, congenital dysplasia, and the scars of malignant hypertension as conditions which might produce these histological changes. *H. Caplan*

IMMUNOPATHOLOGY

892. **Immunological Differences between Normal and Malignant Cells**
R. C. NAIRN, H. G. RICHMOND, M. G. MCENTEGART, and J. E. FOTHERGILL. *British Medical Journal* [*Brit. med. J.*] **2**, 1335–1340, Nov. 5, 1960. 7 figs., 21 refs.

In an investigation at Aberdeen University of the immunological differences between normal and malignant cells the authors have demonstrated that the liver and kidney contain organ-specific antigens which are lost or depleted when malignancy develops. The tissue studied came from three sources—rat liver and rat hepatoma (induced with dimethylaminoazobenzene), hamster kidney and hamster renal carcinoma (induced with oestrogens), and normal and malignant human skin. The antigen used from the hamster and human tissues was a crude extract, while that from rat liver and hepatoma was fractionated to consist predominantly of endoplasmic reticulum (microsome fraction). Antisera obtained in rabbits to these antigens was tested both before and after absorption of non-organ-specific antibodies by three methods: complement-fixation, gel-diffusion analysis, and the use of fluorescent dye conjugates on fresh unfixed frozen sections.

Complement-fixation titre and gel-diffusion analysis combined with tissue absorption studies showed that in both rat liver and hamster kidney the antigens prepared contained at least three components, two of which could be absorbed by antigen extracts of other organs. The organ-specific antigen in each case was either absent or was present only in small amounts in malignant tumour tissue. The same general result was obtained from the gel-diffusion studies of human skin material.

Fluorescent conjugate staining of normal liver, kidney, and skin from these sources showed staining, particularly of cell surfaces and in the perinuclear zones. Malignant tumour cells stained poorly or not at all after non-organ-specific antibodies had been absorbed.

It is suggested that these findings conform with the concept that malignant tumour cells are defective in certain proteins that may be concerned with the control of cellular growth. *J. B. Cavanagh*

893. **Differences in Staining of Normal and Malignant Cells by Non-immune Fluorescent Protein Conjugates**
R. C. NAIRN, H. G. RICHMOND, and J. E. FOTHERGILL. *British Medical Journal* [*Brit. med. J.*] **2**, 1341–1343, Nov. 5, 1960. 8 refs.

The authors, at the University of Aberdeen, examined the claim of Hughes *et al.* (*Nature* (*Lond.*), 1957, **180**, 289) that normal serum globulin conjugated with fluorescein differentially stains normal and malignant tumour tissue. The dye lissamine rhodamine B 200 was conjugated with normal rabbit globulin and used to stain fresh frozen sections of normal and malignant tissue from eight different human organs as well as tissue from animal tumours. There was variable and unpredictable staining from one tissue or tumour to another. Sometimes tumour tissue stained better than normal tissue, but more commonly the reverse took place. The material stained appeared to be the soluble cytoplasmic components and the staining resembled that produced by acid dyes. The authors state that the technique cannot be regarded as a useful method of distinguishing normal from malignant cells. *J. B. Cavanagh*

894. ***In vitro* Investigations of Two Types of Lupus Erythematosus Plasma Factor**
G. BENCZE and L. LAKATOS. *British Medical Journal* [*Brit. med. J.*] **2**, 1571–1572, Nov. 26, 1960. 5 refs.

Previous studies at the University Medical School, Szeged, Hungary, have shown that the L.E. factor from some, but not all, patients with systemic lupus erythematosus (S.L.E.) can be transferred to human beings or animals by plasma transfusion. The present experiments further distinguish the transferable from the non-transferable type of L.E. factor.

Plasma from 8 cases of S.L.E. proved non-transferable, and these plasma specimens produced abundant L.E. cells when mixed with the corresponding patient's leucocytes, but few or no L.E. cells when added to leucocytes from healthy subjects. On the other hand 5 S.L.E. patients donated plasma containing transferable L.E. factor, and these specimens produced many L.E. cells with leucocytes from the patients as well as with leucocytes from healthy donors.

[The quantitation of L.E.-cell tests is unsatisfactory and provides only suggestive evidence.] *M. Wilkinson*

Microbiology and Parasitology

895. **Hemagglutinating Virus Isolated from Cat Scratch Disease**

W. TURNER, N. J. BIGLEY, M. C. DODD, and G. ANDERSON. *Journal of Bacteriology* [*J. Bact.*] **80**, 430–435, Oct., 1960. 1 fig., 3 refs.

In experiments carried out at Ohio State University, Columbus, it was found that allantoic fluid from eggs which had earlier been inoculated with pus from infected lymph nodes from cases of cat-scratch disease agglutinated erythrocytes from rabbits and from hooded rats. Zoning phenomena suggested that an inhibitor was present in allantoic fluid and both the haemagglutinin and the inhibitor appeared to be sensitive to ionic concentration. The inhibitor was removed by diluting allantoic fluid with 0·28 M glucose and centrifuging. Normal rabbit and human sera also contained an inhibitor, which was eliminated by extracting with acetone and reconstituting the serum proteins in a phosphate buffer–hydrochloric acid mixture. Reconstituted sera from immunized rabbits and from 2 out of 3 human cases of cat-scratch fever specifically inhibited haemagglutination. Rabbits did not produce specific antibody after immunization with haemagglutinating fluids unless the fluids had been treated with glucose to remove the inhibitor.

Herpes simplex antiserum was found to inhibit the haemagglutination. However, the haemagglutinating virus did not kill chick embryos even after passage, " had no cytopathogenicity for cells in tissue culture " [no details given], and did not cause lesions on the rabbit cornea. *Janice Taverne*

896. **Virological Studies in Natural Common Colds in Sheffield in 1960**

D. HOBSON and G. C. SCHILD. *British Medical Journal* [*Brit. med. J.*] **2**, 1414–1418, Nov. 12, 1960. 1 fig., 9 refs.

Work at the Virus Research Laboratory, Sheffield, has confirmed the observations made at the Common Cold Research Unit, Salisbury, on the unusual environmental conditions necessary for the production of a cytopathic effect in human-embryo-kidney and monkey-kidney tissue cultures by the H.G.P. strain of virus. This was originally isolated from an individual suffering from a cold and is one of a group of viruses whose cultivation is achieved only by incubation at 33° C. in low-bicarbonate medium with constant rotation of the cultures. These viruses have been designated " Salisbury viruses " and have been shown to produce coryza when inoculated into human volunteers. The study of these agents has been further advanced by the isolation from 25 cases of natural coryza in Sheffield of 8 further strains with these cultural requirements. Seven of the 8 isolates could be propagated only in human-embryo tissue culture and thus resembled the F.E.B. prototype Salisbury virus. Serological comparison could not be undertaken, as no anti-F.E.B. serum was available. The remaining isolate, designated 30/60, resembled the H.G.P. prototype Salisbury virus in that it could be cultivated both on monkey-kidney and human-embryo tissue cultures. It was, however, serologically distinct from the H.G.P. strain. Both the H.G.P. and 30/60 viruses were observed to be capable of isolation and propagation in a continuous line of human epithelial cells, H.Ep.II, with the production of cytopathic effect. Inoculation of H.Ep.II cultures with F.E.B. virus or virus resembling it failed to produce any cytopathic change. Paired sera from 5 of the 8 cases, when examined in neutralization tests, showed a rise in homologous antibody titre. *J. E. M. Whitehead*

897. **The Addition of *para*-Aminobenzoic Acid or Catalase to Löwenstein–Jensen Medium and the Effect of Prolonged Incubation in the Culture of Tubercle Bacilli**

T. V. SUBBAIAH, J. B. SELKON, A. L. BHATIA, D. A. MITCHISON, and S. RADHAKRISHNA. *Tubercle* [*Tubercle (Lond.)*] **41**, 334–340, Oct., 1960. 17 refs.

The authors have considered the possibility that negative cultures from specimens obtained from tuberculous patients under treatment might be due to the carrying over in the sputum of sufficient *p*-aminosalicylic acid (PAS) to inhibit growth; and also that the growth of isoniazid-resistant, catalase-negative mycobacteria might be inhibited by the production of hydrogen peroxide in the culture.

In two investigations at the Tuberculosis Chemotherapy Centre, Madras, 1,792 specimens of sputum were obtained from tuberculous patients receiving isoniazid plus PAS and 2,022 specimens from patients mostly receiving isoniazid alone. The specimens were homogenized with 4% sodium hydroxide, and the centrifuged deposit was then washed with 10 to 15 ml. of distilled water and a loopful inoculated on to Löwenstein–Jensen medium containing no potato starch. Cultures were made from specimens from both groups on to plain medium and medium into which 2 μg. of beef catalase had been diffused just before inoculation. In addition, specimens from the first group were inoculated on to medium containing 10 μg. of *p*-aminobenzoic acid (PABA) per ml. to antagonize the action of PAS. Cultures were incubated at 37° C. and examined at weekly intervals for 8 to 9 weeks.

It was found that neither the amount nor the speed of growth was affected by the addition of catalase or of PABA in those cultures which were positive, the failure to achieve a difference by the addition of PABA being attributed to the removal of PAS from the sputum deposit by washing. In the case of 1,138 sputa the time of incubation was prolonged from 8 to 9 weeks to 16 to 17 weeks, with an increase in the percentage of positive cultures from 39·1% by only an additional 0·4%.

John M. Talbot

898. **The Susceptibility to Hydrogen Peroxide of Indian and British Isoniazid-sensitive and Isoniazid-resistant Tubercle Bacilli**

T. V. SUBBAIAH, D. A. MITCHISON, and J. B. SELKON. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 323–333, Oct., 1960. 1 fig., 19 refs.

This paper from the Tuberculosis Chemotherapy Centre, Madras, describes in considerable detail the technique of a test to estimate with accuracy the proportion of catalase-positive and catalase-negative organisms in strains of tubercle bacilli containing a mixture of both. The test is a modification of that of Kreis and Le Joubioux (*Ann. Inst. Pasteur*, 1957, **92**, 123) using hydrogen peroxide, which is more rapidly bactericidal to catalase-negative than to catalase-positive strains of the bacillus.

This peroxide sensitivity test was applied to (1) 8 British and 7 Indian isoniazid-sensitive, catalase-positive strains, and (2) 13 British and 11 Indian isoniazid-resistant strains. In the first group all the British strains were uniformly susceptible to peroxide, with a 67% survival rate, while 4 of the Indian strains appeared more susceptible, with an average survival rate of 35%. In the isoniazid-resistant group 6 of the British strains were entirely susceptible, while the remaining 7 appeared moderately resistant (average survival rate 23%). There was evidence among the Indian strains in this group of a good deal of catalase activity, and it is suggested that the isoniazid-sensitive Indian strains with increased peroxide susceptibility might be yielding catalase-positive isoniazid-resistant mutants, also with increased susceptibility. An association was found, more marked in British than in Indian strains, between low catalase activity, high susceptibility to peroxide, and a high degree of resistance to isoniazid. *John M. Talbot*

899. **Bacteriological Aspects of the So-called Tuberculomas of the Lung.** [In English]

G. SANTOPADRE and P. F. DELLE SEDIE. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **39**, 97–114, 1960. 39 refs.

The authors of this paper from the University of Pisa have been attracted by the problem of virulence and drug resistance in tubercle bacilli present in tuberculomata of the lung and have noted from reports in the literature that organisms are often seen microscopically but cannot be cultured, indicating that their viability is low. They have investigated in detail 22 tuberculomata of the lung resected from 13 patients at Leghorn Hospital. As well as bacteriological studies of the tuberculoma material they have also carried out cultural and microscopical investigation of the sputum and gastric and bronchial lavage fluid from all the patients.

They found 11 of the tuberculomata to be microscopically negative for acid-fast bacilli. In those that were positive the growth obtained on culture was generally very much less dense than might have been expected from the number of acid-fast bacilli observed in the direct smear, whereas the microscopical and cultural findings in sputum and lavage material corresponded closely. A substantial proportion of tuberculomata were found to be positive for acid-fast bacilli on direct examination alone. The antibiotic resistance of bacilli recovered from a tuberculoma was similar in pattern to that of those from sputum and washings, being generally high for streptomycin and isoniazid. The virulence as determined in the guinea-pig was, however, much lower (1 in 10 or more) than that of organisms obtained by lavage from the same patient.

The authors do not draw any definite conclusions from their work, but consider that the incidence of tuberculomata is related to the use of antibiotics and that the viability or otherwise of organisms in the tuberculoma is related to the age of the lesion. *John M. Talbot*

900. **Attempts to Produce Resistance in Treponemes to Penicillin and Oxytetracycline *in vitro*.** (Versuche an Treponemen zur Erzeugung einer Resistenz gegen Penicillin und Terramycin in vitro)

U. BERGER and H. MARGGRAF. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **210**, 400–408, 1960. 2 figs., 25 refs.

Although there is no clinical evidence of the appearance of strains of *Treponema pallidum* resistant either to penicillin or to members of the tetracycline group of antibiotics, the possibility of such a development has been considered by many workers. The present authors, working in the bacteriological laboratories of the Faciomaxillary Unit of the University of Hamburg, describe in detail the technique of experiments in which the Reiter strain of *T. pallidum* was used and in which they succeeded in increasing one hundredfold the resistance of certain strains of the organism to penicillin, while similar experiments with oxytetracycline resulted in an eightfold increase in resistance. Using two strains of treponeme isolated from the mouth they succeeded in increasing their resistance to penicillin 12- to 50-fold and to oxytetracycline 16- to 22-fold.

[This work is of the utmost theoretical importance and once again points to the conclusion that the indiscriminate use of antibiotics could have serious consequences affecting the future treatment of syphilis.]

R. D. Catterall

901. **Growth Activators for Leptospira.** (К вопросу об активаторах роста для лептоспир (Предварительное сообщение))

I. I. AŠMARIN. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Ž. Mikrobiol.* (*Mosk.*)] **31**, 85–89, Nov., 1960. 9 refs.

From a study of all the available evidence on factors permitting the growth of leptospires *in vitro* it is clear that serum albumin or some of its breakdown products are essential. Of the amino-acids, only thiamine seems to stimulate growth to some extent, so that it appears likely that the presence of breakdown products of the amino-acids, such as indole or indolylacetic acid, is essential for good growing conditions.

In experiments carried out at the Tashkent Postgraduate Institute the potassium salt of indolylacetic acid was chosen for investigation and it was found that the growth of 5 strains of *Leptospira grippotyphosa* was

stimulated very markedly by the addition of this substance to the culture medium. The concentration required for the optimum effect was 0·3 to 0·6 mg. per litre. It was particularly remarkable that one of the 5 strains, which exhibited the phenomenon of poor growth *in vitro* which is so well known in old laboratory strains of *Leptospira*, was restored to its full growth capacity by the addition of the salt in optimum concentration. *K. Zinnemann*

902. **A Simple Fluorescent Stain for Fungi. Selective Staining of Fungi by Means of a Fluorescent Method for Mucin**
J. P. Pickett, C. M. Bishop, E. W. Chick, and R. D. Baker. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **34**, 197–202, Sept., 1960. 9 figs., 4 refs.

Fungi fluoresce red, yellow, yellow-green, or green against a dark background when stained in sections or smears with acridine orange and examined with blue light. The method permits rapid scanning of material for the presence of fungi. The method is simple, requires only 10 to 15 minutes, and can be used in a routine histopathology laboratory. The method demarcates an outer layer and an inner wall of the capsule of *Coccidioides immitis*, as has been observed by histochemical and electron microscopic methods.—[Authors' summary.]

SEROLOGY AND IMMUNOLOGY

903. **The Antibody Response to Smallpox Vaccination as Measured by a Tissue Culture Plaque Method**
E. Cutchins, J. Warren, and W. P. Jones. *Journal of Immunology* [*J. Immunol.*] **85**, 275–283, Sept., 1960. 1 fig., 16 refs.

The measurement of neutralizing antibody response to smallpox vaccination by various test systems has been unsatisfactory because small amounts of residual, uncombined virus can multiply and obscure the result. This can be avoided by use of a tissue culture plaque technique which immobilizes the spread of residual active virus. It has been found that a successful primary vaccination elicits a uniformly good response as measured by both neutralization and hemagglutination-inhibition. In contrast, revaccination provokes a greater elevation in the neutralizing titer and this rise appears to be related to the circulating antibody level at the time of revaccination.—[Authors' summary.]

904. **Transient Appearance of "Autoimmune" Antibodies during Prophylactic Immunization**
E. Hackett and M. Beech. *Journal of Immunology* [*J. Immunol.*] **85**, 533–538, Nov., 1960. 1 fig., 8 refs.

This report from the Institute of Medical and Veterinary Science, Adelaide, describes the results of "autoimmune" complement-fixation (A.I.C.F.) tests carried out with human tissue extracts on sera from 7 healthy nurses during a period of prophylactic immunization against poliomyelitis, tetanus, and typhoid and paratyphoid fevers with Salk vaccine, tetanus toxoid, and T.A.B. vaccine respectively. The tests were performed with extracts of human adrenal gland, liver, kidney, thyroid gland, and lung, Gadjusek's technique being used with minor modifications, on sera obtained before immunization and subsequently at weekly intervals for 7 weeks. The immunization schedule covered 6 weeks.

Every subject showed a satisfactory rise in the titre of antibodies agglutinating typhoid and paratyphoid organisms, the titres reached ranging from 1:2,500 to 1:10,000. One gave positive A.I.C.F. reactions with adrenal, liver, kidney, and lung extracts both before and during the period of immunization, but one year later gave a positive reaction with kidney only. Two subjects gave transient positive A.I.C.F. reactions with all 5 tissue antigens used, the reactions being strongest during the 2nd to the 4th week of the immunization schedule. Sera from each of these 2 subjects were also shown by the tanned-cell haemagglutination test to contain thyroglobulin-reacting antibodies both before and during immunization, whereas those from the remaining 5 subjects did not.

The nature of the mechanism underlying the appearance of transient positive A.I.C.F. reactions in these 2 cases is debatable, but an explanation based on Burnet's clonal selection theory is suggested. Thus it is postulated that there may have been a constitutionally weak "homeostatic mechanism" in these subjects which was temporarily unbalanced during the immunization procedures so that "forbidden clones" of cells were allowed to proliferate and produce "autoantibodies".

Hewett A. Ellis

905. **Preparation of a Stable Non-infective Complement-fixing Antigen for Herpes Simplex**
J. R. Polley. *Canadian Journal of Microbiology* [*Canad. J. Microbiol.*] **6**, 515–518, Oct., 1960. 4 refs.

From the Virus Laboratories, Department of National Health and Welfare, Ottawa, the author describes the preparation of a non-infective soluble antigen of herpes simplex, as follows. Herpes simplex complement-fixing (C.F.) antigen, prepared by macerating infected chick chorio-allantoic membranes in saline and centrifuging to remove gross particles, was allowed to stand at 4° C. for 4 days and then centrifuged at 9,000 *g* for one hour. This speed had been found to remove most of the non-specific C.F. antigens without substantially reducing the amount of herpes C.F. antigen.

Experiments on inactivation with formaldehyde showed that non-infective C.F. antigens of highest titre were obtained either by using low concentrations of formaldehyde at 37° C. for a short time or, alternatively, higher concentrations at 4° C. for a longer time. Antigenicity was best preserved at a high *p*H rather than at the low *p*H which is optimum for influenza virus. The method finally adopted was to treat the antigen with 0·01% formaldehyde at 37° C. for 2 days at *p*H 8·5, neutralizing excess formalin with 30% dibasic ammonium phosphate. The antigen thus obtained withstood freeze-drying and was stored without loss of potency for one year at 4° C.

Janice Taverne

906. **The Reticulo-endothelial System and Resistance to Bacterial Infection.** [Review Article]
J. G. Howard. *Scottish Medical Journal* [*Scot. med. J.*] **9**, 60–82, Feb., 1961. Bibliography.

Pharmacology and Therapeutics

907. **H-3 (Procaine Hydrochloride) Therapy in Aging Institutionalized Patients: an Interim Report**
J. O. SMIGEL, J. PILLER, C. MURPHY, C. LOWE, and J. GIBSON. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **8**, 785–794, Oct., 1960. 1 ref.

An attempt was made in a double-blind trial at Pinehead Nursing Home and Sanitarium, Pinewald, New Jersey, to test the claim of Aslan (*Therapiewoche*, 1956, 7, 14) that administration of " H–3 " (buffered procaine hydrochloride) reduces biological age. Of 60 geriatric patients with " arthritis, nervous disorders, and senile mental disturbances " 30 were given procaine solution and 30 a control solution, the regimen being alternated after an interval. The authors state that the trial was adversely affected by a notable epidemic of respiratory infection with some deaths. The patients suffered from a variety of pathological conditions and improvement or otherwise was assessed on a score of positive or negative views of the patients and of other observers who were not the same in each case. No objective evidence of improvement or statistical analysis is reported. There were no " cures ", no dramatic incidents, and no side-effects. The results of some haematological and biochemical estimations are appended, but these were not in accord with Aslan's findings. The authors found no evidence in support of the latter's claim that procaine therapy reduces biological age, but they cautiously suggest that " enough potential worth has been revealed to justify continuation of the study ".

[Judgment of H–3 by controlled trials is overdue, but this trial, with its small number of patients suffering from a multiplicity of ailments and without objective estimates of changes in state of health, cannot be considered valid.]

J. N. Agate

908. **Hemodynamic Effects of β Methyl 2:6-Dimethylphenylether of Choline (SKF 6890) on the Systemic and Coronary Circulations**
G. G. ROWE, G. M. MAXWELL, C. A. CASTILLO, J. E. CLIFFORD, and C. W. CRUMPTON. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 409–412, Sept., 1960. 1 fig., 8 refs.

Pharmacological evidence suggests that the β-methyl form of 2:6-dimethylphenylether of choline (SKF 6890), a quarternary nitrogen compound, prevents the release of catecholamines from adrenergic nerve endings. In this paper experimental studies of the haemodynamic effects of this compound are described from the University of Wisconsin, Madison. Special attention was given to comparison of the action of SKF 6890 with that of ganglion-blocking drugs which block both sympathetic and parasympathetic nerves. It was shown that in 10 anaesthetized dogs after administration of SKF 6890 the cardiac output and stroke volume fell, this being accompanied by a fall in the systemic arterial, pulmonary arterial, and right atrial blood pressures, while there was a significant increase in the arterio-venous oxygen and carbon dioxide differences. The coronary arterial blood flow fell, but the cardiac metabolic rate for oxygen was unchanged; cardiac work and efficiency decreased.

The authors point out that these effects are very like those of the ganglion-blocking drugs and refer to the suggestion of Cotten *et al.* (*Anesthesiology*, 1954, **15**, 126) that the decreased cardiac output produced by hexamethonium, for example, is effected through decreased force of myocardial contraction secondary to lowered arterial blood pressure and decreased sympathetic discharge.

David Phear

909. **The Peripheral Dilator Action of Reserpine in Man**
I. S. DE LA LANDE, V. J. PARKS, A. G. SANDISON, S. L. SKINNER, and R. F. WHELAN. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **38**, 313–320, Aug. [received Nov.], 1960. 5 figs., 19 refs.

To study its peripheral dilator action reserpine was introduced into one brachial artery of healthy volunteers at a rate of 50 μg. per minute for 10 minutes. No effect was noted until 10 to 20 minutes after the end of the infusion, when the blood flow in the skin of the forearm began to increase, reaching a maximum in 60 to 90 minutes and returning to normal after 24 hours. No change took place in the untreated control arm. The flow was determined by venous occlusion plethysmography. Simultaneous determinations of oxygen saturation of venous blood in skin and muscle showed that the flow through the muscles was not affected. The dilated skin vessels responded normally to ephedrine or " methedrine " and to noradrenaline. The authors, who report from the University of Adelaide, suggest that the time course of these effects is compatible with the release of noradrenaline and its slow resynthesis in the chromaffin tissue of the peripheral vessels, and that the content of noradrenaline and chromaffin tissues is higher in vessels of skin than of muscle.

V. J. Woolley

910. **Effect of Long-term Treatment with Chlorothiazide on Body Fluids, Serum Electrolytes, and Exchangeable Sodium in Hypertensive Patients**
P. LAUWERS and J. CONWAY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 401–408, Sept., 1960. 2 figs., 15 refs.

It has been shown that during the first week of treatment with chlorothiazide the urinary volume increases, the body weight and blood pressure fall, and there is also a fall in blood volume, with loss of body sodium. The study of the changes in body fluid and serum electrolyte levels during long periods of treatment with chlorothiazide here reported from the University of Michigan Medical Center, Ann Arbor, was carried out on 15

hypertensive patients whose diastolic blood pressure was at least 100 mm. Hg and who were treated with 1 g. of chlorothiazide daily for 26 to 60 days. They were asked not to add salt to their food, but otherwise took a normal diet without potassium supplements.

The body weight fell within 48 hours and remained at the lower level, the average weight loss in the 15 patients being 2·1 kg., while there was a consistent decrease in total body water averaging 1·8 litre. The mean changes in extracellular fluid (which rose by a mean of 200 ml.) and plasma volume (which decreased by 51 ml.) were insignificant, and it is therefore concluded that the loss of body water and body weight must have resulted from loss of intracellular fluid. This intracellular dehydration could be due either to a direct effect of the chlorothiazide, or alternatively it might result from potassium depletion —although the average fall in the serum potassium level was only 0·4 mEq. per litre. The values for serum sodium concentration and total exchangeable sodium were unchanged. The slight fall in plasma volume observed (51 ml.) was associated with a mean fall in blood pressure of 24/13 mm. Hg. It is suggested that the hypertensive action of chlorothiazide may result from a decrease in arteriolar muscle tone due to intracellular dehydration. *David Phear*

911. **Hydrochlorothiazide Used Alone in Congestive Heart Failure and in Combination with Prednisone and Other Diuretics in Cirrhosis and Nephrosis**

G. A. Porter and N. A. David. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 417–432, Oct., 1960. 3 figs., 39 refs.

The authors report, from the University of Oregon Medical School, Portland, their experience in the short-term use of hydrochlorothiazide in 20 patients, of whom 11 had congestive heart failure, 8 hepatic cirrhosis, and one nephrosis. The patients were first stabilized for a period of 3 days by means of bed rest and a restricted-sodium diet, after which hydrochlorothiazide was administered in a dosage of 50 to 100 mg. three times daily for 6 to 14 days.

All 11 patients with congestive heart failure responded to the diuretic as shown by loss of body weight, increased output of urine, and a rise in urinary sodium excretion as compared with the control period. Urinary potassium excretion was also increased in these patients. Of the 8 patients with cirrhosis, 4 failed to respond to hydrochlorothiazide alone, but in 2 of these an increase in urinary volume and sodium output was achieved when prednisone (10 mg. 8-hourly) was added to the therapeutic regimen. The patient with nephrosis responded poorly to hydrochlorothiazide alone, but she also had an excellent diuresis when prednisone was given in addition. In regard to the cirrhotic patients, other measures such as chloride loading with calcium or potassium chloride for 3 to 5 days, the simultaneous administration of hydrocortisone and a mercurial diuretic, or alternation of hydrochlorothiazide with a mercurial diuretic or acetazolamide did not lead to an improvement in response of the 4 who were refractory to treatment with hydrochlorothiazide with prednisone. *M. Harington*

912. **Determination of the Toxicological and Pharmacological Properties of Carbocaine, Lidocaine and Procaine by Means of Simultaneous Experiments.** [In English]

F. Henn. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **4**, 125–154, 1960. Bibliography.

The toxicological and pharmacological properties of " carbocaine ", lidocaine [lignocaine] and procaine were tested in simultaneous experiments on animals and man. Test methods recommended by other investigators were used; the experiments were performed by the " blind " or " double-blind " method, and the results were subjected to statistical analysis. The results obtained are compared with those published by other investigators.

It appeared that procaine has the lowest toxicity of the three local anaesthetics studied. The conclusion of the toxicity tests performed was that carbocaine is somewhat less toxic than lignocaine, in particular, when low—that is sublethal, therapeutic—doses are administered. In surface anaesthesia of the rabbit cornea, in infiltration anaesthesia in guinea-pigs and man, and in conduction anaesthesias of various types, carbocaine proved to be the most effective drug, followed by lignocaine and procaine in that order. In tests with adrenaline-containing solutions of the three local anaesthetics, the difference between the anaesthetic effects of carbocaine and lignocaine was not always significant.

The clinical value of a local anaesthetic is determined by its toxicological and anaesthetic properties. As lignocaine has proved to be an excellent local anaesthetic although it is more toxic than procaine, the results obtained suggest that carbocaine may in time be recognised as a still better drug. Whether it is permissible from the results obtained to conclude that carbocaine represents a new conquest in the field of local anaesthesia can obviously be decided only on the basis of the experience gained when it has been used under variable clinical conditions for several years.—[From the author's summary.]

913. **Lack of Relationship between Inhibition of Monoamine Oxidase and Potentiation of Hexobarbital Hypnosis**

M. J. Laroche and B. B. Brodie. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol. exp. Ther.*] **130**, 134–137, Oct., 1960. 8 refs.

A number of monoamine oxidase inhibitors prolong the duration of barbiturate hypnosis. In an experimental study at the National Institutes of Health, Bethseda, Maryland, mice were anaesthetized with hexobarbitone and the effect on sleeping time of four monoamine oxidase inhibitors was studied.

Monoamine oxidase inhibition started rapidly and lasted for many hours after the drugs had disappeared from the body. Prolongation of barbiturate sleeping time, however, was relatively short-lived and lasted only about an hour. A small dose of one monoamine oxidase inhibitor (" JB 516 ") completely blocked monoamine oxidase activity but did not prolong hexobarbitone hypnosis, while another drug (" SKF 525-A ") in suitable dosage prolonged hypnosis without inhibiting monoamine oxidase activity. The authors state that the two

effects of these drugs are independent and that experiments *in vitro* with liver homogenates have confirmed this. Monoamine oxidase inhibitors do not render the central nervous system more sensitive to hexobarbitone since pretreated mice wake after a longer sleep with the same body concentration of barbiturate as untreated mice. The prolonged duration of hexobarbitone hypnosis must, therefore, be due to slowing of metabolic transformation of hexobarbitone. *M. Woods*

914. **Accidental Ingestion and Overdosage Involving Psychopharmacologic Drugs**
H. M. CANN and H. L. VERHULST. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 719–724, Oct., 13, 1960. 33 refs.

This paper reviews the records of 280 cases of accidental poisoning with " tranquillizer " drugs reported to the National Clearinghouse for Poison Control Centers, Washington. Of the drugs ingested, phenothiazine derivatives constituted 31·8%, rauwolfia alkaloids 28·2%, and mild tranquillizers such as meprobamate and hydroxyzine 40%. Children under 5 years of age accounted for two-thirds of the cases involving phenothiazine, 96% of those due to rauwolfia alkaloids, and slightly less than one-third of those due to meprobamate. Adults accounted for 62% of the cases for which meprobamate was responsible. No deaths were reported. Toxic effects were noted in 45% of cases, mostly in adults. Mild and serious central nervous depression, hypotension, convulsions, and extrapyramidal symptoms occurred after the ingestion of phenothiazine derivatives; rauwolfia gave rise to mild depression and flushing, while meprobamate caused mild depression, coma, and hypotension. Benactyzine, phenaglycodol, and hydroxyzine also caused mild central nervous depression. The authors discuss the various forms of therapy used in these cases. *I. Ansell*

915. **The Use of " Testobromlecit " in Clinical Practice.** (Опыт применения тестобромлецита в клинической практике)
B. A. VARTAPETOV and L. M. ŠIFMAN. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Êndokr. Gormonoter.*] **6**, 112–115, Nov.–Dec., 1960. 10 refs.

" Testobromlecit ", a preparation devised by the first-named author, is a combination of methyltestosterone with bromural and lecithin. A course of treatment consists of 3 or 4 tablets daily for 3 weeks, followed by 1 or 2 a day for a similar period; this course can be repeated if necessary two or three times a year. Of 72 patients so treated for " involutional hormone deficiency", 10 were aged from 45 to 50, 26 from 51 to 55, 20 from 56 to 60, and 16 from 61 to 65. Most of them had complained for one to 3 years of weakness, giddiness, failing memory, sleep disturbances, precordial pain, sweating, attacks of " flushing " and heat in the head or neck, and reduced libido and sexual potency. They could be divided into three groups: (1) those with predominantly mental changes, (2) those with neurovascular symptoms, and (3) those with cardiovascular symptoms. The disturbances of the vegetative nervous system were not necessarily associated with the presence of arterial hypertension, though transient hypertensive attacks were common.

The blood cholesterol level was raised in most (66) of the patients. Treatment with testobromlecit lowered this level considerably, in 59 cases to below 200 mg. per 100 ml. at the end of the course. It also relieved the depression, insomnia, sweating, and neuro-vascular symptoms and diminished the frequency of the hypertensive attacks. The permanently hypertensive patients, however, obtained less relief than the others. No ill-effects of the drug were observed, but the treatment was not given to patients with prostatic enlargement or to those in whom the psychasthenic disturbances were not associated with hormonal insufficiency.
L. Firman-Edwards

916. **The Antigoitrogenic Effect of " Betazine ".** (Антиструмогенное действие бетазина)
S. I. HARLAMPOVIČ. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Êndokr. Gormonoter.*] **6**, 65–69, Nov.–Dec., 1960. 6 figs., 3 refs.

" Betazine ", one of the synthetic analogues of diiodotyrosine with the formula 3-amino-4:6-diiodophenyl-β-alanine dichlorhydrate, was employed by the author in conjunction with methylthiouracil in experiments on young male rats in order to assess its ability to prevent the goitrogenic effect of the latter, an effect which is only partially controlled by potassium iodide.

One group of animals received betazine alone in a dosage of 15 mg. per 100 g. body weight daily, a second group received 3 mg. of methylthiouracil per 100 g. alone daily, a third group was given both drugs in the above daily dosage, while a fourth, untreated, group acted as a control. The experiment lasted 30 days and on the 5th, 10th, 20th, and 30th days respectively 5 rats in each group were killed, the thyroid and pituitary glands excised, and their weight in relation to the body weight calculated. In addition, sections of the glands were prepared for histological examination.

The rats receiving betazine alone showed an enhanced rate of growth as compared with controls, and the ratio of thyroid weight to body weight fell from 19·7% at 5 days to 12·6% at 30 days, compared with 17·1% and 12·4% in the controls. The weight of the hypophysis was unchanged. Those given methylthiouracil alone showed a smaller gain in weight over the 30 days, and the relative weight of the thyroid gland was three times that of the controls, while that of the hypophysis was slightly raised compared with the controls. The third group showed a still smaller gain in body weight, a much smaller increase (50%) in the relative weight of the thyroid gland, and a greater increase in the relative weight of the hypophysis. Histologically, the sections of the thyroid glands showed in the first group a progressive increase in the height of the epithelium and vacuolation of colloid. Those of the third group, in comparison with those of the second, showed follicles filled with colloid, much lower epithelium, and much less hyperaemia. The author concludes that betazine effectively controls the " goitre effect " of methylthiouracil.
L. Firman-Edwards

Chemotherapy

917. **Role of Kanamycin in the Management of Infections**

G. M. Koota, F. B. Schweinburg, and A. M. Rutenburg. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 629–633, Sept. 29, 1960. 34 refs.

The authors of this paper from Beth Israel Hospital, Boston, report their experience of kanamycin in the management of 163 patients suffering from surgical, urinary, and respiratory infections due to staphylococci and various Gram-positive and Gram-negative bacteria, many of which were resistant to other antibiotics. The drug was given intramuscularly in a dosage of 1 g. initially, 0·5 g. every 6 hours for 48 hours, and then 0·5 g. every 12 hours for 4 to 5 days. Of the 163 patients, 25 also received the drug intravenously and 12 intraperitoneally. Kanamycin was well tolerated whatever the route of administration in all except 14 patients. In 13 of these, granular casts appeared in the urine in 2 to 4 days but cleared within 5 days of discontinuing the drug, while in the remaining patient a permanent hearing loss of 40 decibels and temporary renal insufficiency developed after intravenous administration of 2 g. daily for 12 days. Hyaline casts were observed in the urine of several patients, but no other evidence of systemic or local toxicity was found. Respiratory depression was not noted during anaesthesia.

Infections of postoperative wounds, soft tissues, the respiratory and urinary tracts, peritoneum, and blood stream responded favourably to kanamycin therapy in 138 of the 163 patients, 69 of whom had failed to respond to other antibiotics. Most failures occurred in cases of soft-tissue and urinary-tract infections. Infections due to staphylococci, *Escherichia coli*, and *Aerobacter aerogenes* were particularly responsive, while those due to *Proteus vulgaris* and *Pseudomonas* were more refractory.

The authors state that kanamycin has a useful place in the management of infections due to certain Gram-positive and Gram-negative organisms, but that rigid control of the daily dosage and duration of therapy, appropriate laboratory studies, and close clinical observation are essential. *A. Ackroyd*

918. **Cyclophosphamide: a Preliminary Study of a New Alkylating Agent**

L. V. Foye Jr., C. G. Chapman, F. M. Willett, and W. S. Adams. *Archives of Internal Medicine* [*Arch. intern. Med.* (*Chicago*)] **106**, 365–367, Sept., 1960. 7 refs.

A brief clinical trial of cyclophosphamide, a new alkylating agent, is reported. The agent was administered intravenously, orally, intrapleurally, and intraperitoneally in various doses to patients with advanced malignancies. The toxic effects observed included severe anorexia, with occasional nausea; leukopenia of moderate severity which was rapidly reversible upon cessation of therapy but which recurred upon its resumption; and an occasional case of patchy alopecia which was therapeutically of no significance. The occurrence of toxic and beneficial effects appeared to be independent of the route of administration. In 8 of 25 evaluable patients there appeared to be definite antitumour effects. —[Authors' summary.]

919. **Vincaleukoblastine. I. Preliminary Clinical Studies**

M. E. Hodes, R. J. Rohn, and W. H. Bond. *Cancer Research* [*Cancer Res.*] **20**, 1041–1049, Aug., 1960. 5 figs., 4 refs.

Clinical trials of vincaleukoblastine, a new alkaloid from *Vinca rosea* Linn., in 22 patients, including 8 with leukaemia, 5 with malignant lymphoma, and 9 with other malignant tumours, are described from Indiana University Medical Center, Indianapolis. The toxic effects encountered were: local effects of injection (pain, numbness, and tingling, and 3 patients developed thrombophlebitis); general effects, such as weight loss, nausea, and symptoms referable to the nervous system. Severe granulocytopenia with little or no depression of platelet count was noted in most cases. In 15 of the 22 cases the drug had measurable effects on the malignant process. Partial remissions of short duration, with marked improvement in general condition, were obtained in 3 children with acute leukaemia, in one patient with lymphosarcoma, and in one with breast cancer.

[See also Abstract 872.] *L. A. Elson*

920. **Therapeutic Spectrum of Uracil-mustard, a New Oral Antitumor Drug. With Special Reference to the Effects of Small Dosage in Lymphomas, Chronic Leukemias, and Ovarian Carcinoma**

E. Shanbrom, S. Miller, H. Haar, and R. Opfell. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 1702–1705, Nov. 26, 1960. 9 refs.

The authors report the results of treatment, at Orange County General Hospital, Orange, California, of 100 cases of haematological neoplasia and 30 cases of solid tumours by administration of uracil-mustard. This is a new oral alkylating agent in which the mustard radical has been attached to the pyrimidine precursor, uracil. Treatment was given at intervals over periods as long as 16 months.

The best responses were obtained in cases of lymphoma and of chronic leukaemia; some ovarian tumours also gave a good response. The advantages of uracil-mustard over similar agents are said to be: " (1) the small dosage required to obtain beneficial results; (2) uniform tolerability; and (3) simplicity of the regimen ". It is suggested that this agent may be of use when other agents have failed. *G. Calcutt*

Infectious Diseases

921. **Bedbugs as a Possible Reservoir of *Rickettsia burneti*.** (Постельный клоп как возможный резервуар риккетсий Бернета (Экспериментальные и эпидемиологические данные))
A. B. DAJTER. *Вопросы Вирусологии* [*Vop. Virusol.*] **6**, 591–598, Sept.–Oct., 1960. 3 figs., 15 refs.

The author reports from the Pasteur Institute for Epidemiology, Leningrad, that in experimental conditions bed-bugs in all postembryonal stages can be infected with *Rickettsia burneti* by feeding on infected guinea-pigs. In these studies two strains of *R. burneti* were used, the Italo–Greek strain *Grita* and Strain 422 isolated in Czechoslovakia. The organism is able to pass through the metamorphotic cycle of the bed-bug. At temperatures of 19° and 30° C. it was observed to remain viable and virulent in this host for up to 285 days, when the observations were discontinued. During its stay in the bed-bug *R. burneti* appears to multiply and is excreted in the faeces. The pathogen was isolated in 6 instances from bed-bugs in an endemic focus of Q fever in the Luga District near Leningrad, two strains thus isolated being passaged through guinea-pigs and adapted to chick embryo culture. It is suggested that future work will have to be directed towards confirming the transmission of Q fever to man by bed-bug. If this should be proved then anti-Q-fever measures would have to include disinfestation action against bed-bugs.

K. Zinnemann

922. **Potassium in the Treatment of Cholera**
R. H. WATTEN and R. A. PHILLIPS. *Lancet* [*Lancet*] **2**, 999–1001, Nov. 5, 1960. 2 figs., 20 refs.

Potassium depletion in cholera was studied in 17 patients with the acute form of the disease seen during the epidemic in Bangkok in 1958. For the first 24 hours after the patients were admitted to hospital all fluid was given intravenously, balance studies being carried out in the meantime. The patients passed 3 to 17 litres of faeces in 24 hours, the mean potassium content of the faeces being 16 mEq. per litre. During the period of diarrhoea, therefore, 15 to 30% of the total exchangeable body potassium was lost in the urine and faeces. While this acute phase lasted plasma potassium levels were no guide to the degree of depletion.

The authors state that deficiency of potassium frequently leads to paralytic ileus, with cessation of diarrhoea and abdominal swelling. This sequestration of large volumes of fluid in the bowel is dangerous if fluid therapy is based only on the replacement of observed faecal volumes. Depletion of potassium in cholera may also cause a moderate alkalosis, changes in the electrocardiogram, renal tubular damage, and neuromuscular disturbances. The most important factor in the treatment of acute cholera is the prompt replacement of lost water and electrolytes. After the initial rapid infusion of fluid to combat shock and collapse the addition of potassium to the replacement solution would be advantageous. The authors recommend adding 10 mEq. (7·5 g.) of potassium chloride to each litre of replacement fluid. Such a fluid could be given with safety in remote areas and would replace at least half of the initial potassium loss; it should be given as long as fluid loss from the bowel continues.

L. G. Goodwin

923. **Is Universal Vaccination against Pertussis Always Justified?**
J. STRÖM. *British Medical Journal* [*Brit. med. J.*] **2**, 1184–1186, Oct. 22, 1960. 23 refs.

In Sweden, as in several other countries, neurological complications after pertussis (triple) vaccination have been observed. A nation-wide investigation showed that 36 cases of such complications had occurred in about 215,000 vaccinated children (1 in 6,000) during 1955–8. Most of these consisted of convulsions, coma, or collapse, and the children were restored to health; but there were 4 deaths, of which 2 were sudden, and 9 cases indicative of encephalopathies with severe lesions (1 in 17,000). An investigation of the incidence of neurological complications after pertussis showed that this was not so high as after vaccination. The increasingly mild nature of whooping-cough and the very low mortality in this disease in Sweden makes it questionable whether universal vaccination against it is justified. The same question may perhaps arise in some other countries.—[Author's summary.]

VIRAL DISEASES

924. **Atypical Clinical Course of Measles.** (Атипичное течение кори)
G. G. BOSTREM. *Советская Медицина* [*Sovetsk. Med.*] **25**, 13–17, Nov., 1960. 7 refs.

Changes in the typical clinical course of infectious diseases are being described with increasing frequency. The causes of this evolution are little understood, but changes in bodily reactivity induced by antibiotics and the natural evolution of the pathogenic organisms have been mentioned as possible factors. During the period 1956–8 50 cases of atypical measles in otherwise normal children aged 1 to 14 years came to the author's notice. A history of a previous mild attack of measles was obtained in 5 cases, while other infectious diseases (dysentery, whooping-cough, or tonsillitis) had occurred immediately before the attack or even during the incubation period in 15. Only 4 patients received antibiotics during the incubation period or during the first few days of the disease. The clinical picture varied, consisting in some cases in a rash only, when the diagnosis depended largely on epidemiological findings.

Three types of case could be distinguished. In Group 1 (28 patients) the clinical course was severe, with marked

toxaemia and pyrexia and a high incidence of complications (50%). The early stages were atypical, the appearance of Filatov's [Koplik's] spots being delayed or absent and catarrhal manifestations being mild or failing to develop at all, while the duration of the prodromal period was altered. Diagnosis in some cases was made more difficult by the presence of various unrelated manifestations, and prophylactic measures were often delayed. In Group II (10 patients) the disease was abortive. The early stages were atypical, as in Group I, there was a marked but short-lived toxaemia (1 or 2 days), and the rash developed rapidly. In Group III (12 patients) the child's general condition remained good, the temperature was normal or only slightly raised, and there were no catarrhal manifestations and no Koplik's spots. The diagnosis in this group rested largely on epidemiological grounds. *S. W. Waydenfeld*

925. **Enterovirus Infections in Manitoba—1959**
J. C. Wilt, W. L. Parker, A. L. Owens, and W. Stackiw. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 839–843, Oct. 15, 1960. 3 figs., 7 refs.

This paper from the Manitoba Virus Laboratory reports a study to correlate clinical features with virological findings in an outbreak of enterovirus infections which occurred in the Canadian Province of Manitoba during 1959. Analysis of specimens, including faeces, rectal swabs, throat swabs and washings, and post-mortem specimens of large bowel, led to the identification of 133 enteroviruses. The predominant types were poliomyelitis Type I (28), E.C.H.O. Type 6 (36), and Coxsackie Group B, Type 5 (45). There were 57 cases of aseptic meningitis caused by E.C.H.O. Type 6 (34), Coxsackie Group B, Type 5 (13), E.C.H.O. Type 20 (4), E.C.H.O. Type 11 (2), E.C.H.O. Type 9 (1), poliomyelitis Type I (2), and poliomyelitis Type III (1). The association between E.C.H.O. virus Type 20 and aseptic meningitis does not appear to have been reported previously, and the 4 case histories are summarized. Paralytic lesions occurred in 19 cases caused by poliovirus Type I. Epidemic myalgia was associated in 18 instances with isolation of Coxsackie virus Group B, Type 5.

All the cases investigated, which represent only a sampling from the more severe infections, occurred between July and October, 1959, the majority in children under 5 years of age. *John Fry*

926. **Infectious Hepatitis: Studies on the Effect of Gamma Globulin and on the Incidence of Inapparent Infection**
S. Krugman, R. Ward, J. P. Giles, and A. M. Jacobs. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 823–830, Oct. 15, 1960. 5 figs., 12 refs.

Between 1956 and 1960 four carefully controlled trials of the effect of gamma globulin on the incidence of infective hepatitis were carried out in an institution in New York for mentally defective children where the disease is endemic. The initial trial established the protective value of a single inoculation of gamma globulin in a dose of 0·01 ml. per lb. (0·02 ml. per kg.) body weight, but subsequent experience indicated that 0·06 ml. per lb. (0·132 ml. per kg.) was superior, leading to a thirty-fold decrease in the incidence of hepatitis. Protection was most obvious during the five months following inoculation and was presumably due to both passive and coincidental active immunization. Inapparent anicteric hepatitis continued in spite of inoculation of gamma globulin and was twelve times more frequent than overt jaundice. "Grumbling" subclinical infections were considered to be responsible for the state of active immunity which developed in the community. *D. Geraint James*

927. **A Comparative Study of the Treatment of Acute Viral Hepatitis.** (Vergleichende Therapie der akuten Virushepatitis)
H. A. Kühn and H. Baur. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 1956–1965, Nov. 4, 1960. 6 figs., bibliography.

This comparative study of the value of certain drugs in the treatment of infective hepatitis was carried out at the Southern City Hospital, Lübeck, in association with many other clinics in West Germany. Altogether, 404 patients were admitted to the trial, but in 38 cases the course of treatment laid down had to be changed owing to a deterioration in the clinical condition, leaving 366 for the final analysis. The diagnostic criteria adopted included a 14-day history and a serum bilirubin level of at least 5 mg. per 100 ml. Comatose and pre-comatose patients were excluded from the trial. The patients' ages ranged from 15 to over 50 years. Progress was judged by the disappearance of subjective symptoms, the duration of jaundice and of hepato- and splenomegaly, and the time taken for the serum bilirubin level to fall below 1·5 mg. per 100 ml.

The basic treatment consisted in rest in bed, a diet rich in carbohydrate and protein but poor in fat, with the addition of vitamin-B complex and ascorbic acid by mouth, and hot moist packs to the upper abdomen thrice daily for 45 minutes. Group I (142 patients) received the basic treatment only, while the remaining patients received various drugs in addition. Group II (48) received one ampoule of "hepsan" intravenously daily for 14 days; this consists of 0·25 g. of acetylmethionine-choline and 1·25 g. of sodium acetylmethionine. Group IIA (17) were given 2 tablets of "litrison" [a mixture of lipotropic factors] thrice daily. Group III received a total of 38 mg. of prednisone in 9 days, followed by 20 units of depot corticotrophin (ACTH) for 3 days. Group IV (15) received a total of 1,100 mg. of BAL intramuscularly over 5 days. Group V (27) received cyanocobalamin (vitamin B_{12}) intramuscularly daily for 3 weeks in diminishing dosage (45 μg. for the first week, 30 μg. for the second, and 15 μg. for the third). Group VI (24) received 1·6 mg. of thiocturic acid intravenously daily for 14 days.

Apart from those in Group III none of the patients receiving additional treatment fared any better than the controls as judged by the initial criteria. In Group III the serum bilirubin and transaminase levels fell more rapidly than in the control group, but the results of other liver function tests were not affected. Although the

action of steroids is non-specific, the authors recommend their use in all serious cases of infective hepatitis, primarily because of their anti-inflammatory action.

I. M. Librach

928. **Antipoliomyelitis Vaccination in Day Nurseries in the Seine Department (1958–60). Importance of Detection of " Silent " Poliomyelitis Infection in Evaluating the Response to Vaccination.** (La vaccination antipoliomyélitique dans les crèches du département de la Seine (1958–1960). Importance du dépistage des contaminations poliomyélitiques inapparentes pour l'appréciation exacte de la réponse sérologique post-vaccinale)
X. LECLAINCHE and J. ZOURBAS. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2739–2752, Nov. 4, 1960. 17 refs.

The serological response of young children to 4 doses of 7 different batches of the Pasteur Institute killed poliomyelitis vaccine was studied in day nurseries in the Seine Department from September, 1958, to May, 1960. Each nursery housed 30 to 50 children aged 3 months to 3 years. The vaccine was administered by subcutaneous injection in 3 doses of 1 ml. at intervals of 3 to 4 weeks followed by a booster injection of 1·5 ml. 6 to 12 months after the third. The number of children vaccinated totalled 960, from all of whom blood samples were collected before vaccination, 2 to 7 weeks after the third dose, and before and after the fourth dose. In evaluating the antigenic potency of the vaccine batches the authors were at pains to detect those nurseries in which infection by wild poliovirus strains occurred before or during the trial. For this they relied on serological observations made simultaneously on unvaccinated control children.

In infants originally " triple-negative " or possessing neutralizing antibody to one type of poliovirus only they found that, in general, the serum antibody content had declined to a low level by 6 months after the third injection and that the occurrence of infection by a single virus type after vaccination did not modify the decline in the titre of antibodies to the heterologous types. The authors emphasize the importance of the fourth dose of vaccine as a means of rapidly eliciting satisfactory antibody titres to all 3 types of virus. *J. E. M. Whitehead*

929. **Disturbances in Nitrogen Metabolism in the Acute Stage of Paralytic Poliomyelitis.** [In English]
I. JUNGNER and G. JUNGNER. *Acta medica Scandinavica* [*Acta med. scand.*] **168**, 169–192, 1960. 12 figs., bibliography.

Nitrogen loss in severe paralytic poliomyelitis was studied in some 30 patients at the Hospital for Infectious Diseases, Stockholm, up to one year after the onset of the disease by analysing the various nitrogenous substances and fractions in the blood and urine.

In the acute stage of the disease the urinary excretion of total nitrogen was very high, indicating a great increase in nitrogen metabolism, and in general showed a good correlation with the degree of severity; the maximum excretion usually occurred in the second week. A constant relationship existed between the urinary output of urea nitrogen and total nitrogen. Excretion of ammonia, amide, and amino nitrogen did not appear to undergo any characteristic changes, but excretion of uric-acid nitrogen increased considerably a few weeks after the onset of paralysis. Creatine excretion showed initially great variations, but the maximum usually coincided with that of the total nitrogen. Creatinine excretion tended to fall steadily for several months often to very low levels, especially in extremely severe cases, but with muscle restitution values began to rise.

In the blood there was also a marked increase in substances which partake in nitrogen transport in the body or are end-products of its metabolism. Despite the load, liver and kidney function were not apparently impaired, rises in non-protein nitrogen levels being due to the greatly increased nitrogen metabolism. In the acute stage of the disease the creatine clearance value rose far above the normal range, while tubular reabsorption almost ceased as a result, probably, of competition with other substances. This, the authors state, explains the discrepancy, noticeable clinically, between the creatine excretion and the degree of paralysis. Analysis of the serum protein components showed that there was a decrease in the serum albumin value, but no changes were found in the other serum proteins that could not be explained as a result of infection.

The authors point out that it is probably not possible to calculate the remaining or functioning muscle mass on the basis of the total nitrogen or creatine or creatinine values in the urine, since unspecific inflammatory processes contribute to forming the chemical pattern of nitrogen metabolism in poliomyelitis. *A. Ackroyd*

930. **Poliomyelitis Epidemic in Mauritius and the Effect of Vaccination**
B. TEELOCK. *British Medical Journal* [*Brit. med. J.*] **2**, 1272–1276, Oct. 29, 1960. 3 figs., 5 refs.

The author gives an account of an outbreak of poliomyelitis due to a Type-1 virus which occurred in Mauritius during June to September, 1959. A total of 97 paralytic cases scattered haphazardly throughout the island were reported in the 14 weeks. The attack rate was 15·6 per 100,000 population, with the maximum incidence in infants under 3 years old and a peak incidence in the 7th to 8th week of the outbreak. It was about the same in the various ethnical groups. There were no deaths, and all cases were isolated individual ones. No drastic preventive measures were taken, but 11 weeks after the onset oral Sabin Type-1 poliovirus vaccine was offered to all children between 6 months and 10 years old; 195,000 of the estimated child population of 213,000 between these ages received the vaccine. Only 4 cases were reported after the start of the vaccination programme.

Compared with previous epidemics the outbreak occurred at an unexpected time of year, during the coldest months. Among the children who had received 3 injections of Salk vaccine during the previous 2 years the incidence was only 2·3 per 100,000, but among the unvaccinated it was 279·1 per 100,000. Since 1945 the incidence and severity in successive outbreaks on the island have been diminishing. *A. Ackroyd*

Venereal Diseases

931. **New and Improved Antigen Suspension for Rapid Reagin Tests for Syphilis**
J. PORTNOY and W. GARSON. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **75**, 985–988, Nov., 1960. 5 refs.

The antigen suspension used for the rapid plasma reagin (R.P.R.) test for syphilis, using unheated plasma or serum, is made by resuspending centrifuged V.D.R.L. slide-test antigen in choline chloride. As originally described (*Publ. Hlth Rep.* (*Wash.*), 1957, **72**, 761; *Abstr. Wld Med.*, 1958, **23**, 254) the suspension was said to be stable for at least a week, but subsequent work at the Venereal Diseases Research Laboratory, Chamblee, Georgia, has shown that some batches remain stable for up to 18 months. It was found that loss of reactivity is due to an oxidative process catalysed by cations.

In this study, undertaken to determine means of preventing this decline in reactivity, a series of antigen suspensions were prepared and contaminated with various cations and hydrogen peroxide and their stability determined by serial tests on pooled reactive human serum, using freshly prepared R.P.R. antigen as a control. On storage at room temperature antigens to which salts of copper, iron, magnesium, or zinc were added lost activity in 1 to 2 weeks, the loss being most rapid with copper sulphate. It was then shown that this deterioration could be prevented by the addition of sodium calcium-edetate (EDTA) as a chelating agent and that this agent was active in inhibiting deterioration for up to 3 weeks in a dilution as low as $1{\cdot}25 \times 10^{-4}$M. In the light of these findings it is recommended that EDTA should be incorporated in R.P.R. antigen suspensions. After precipitating the V.D.R.L. antigen and centrifuging, the deposit should be resuspended to the original volume in a solution composed as follows: 2·5 ml. of 0·1 ml. of 0·1 M EDTA in distilled water (*p*H 7·0), 5 ml. of 40% choline chloride in distilled water, 10 ml. of 0·02 M phosphate buffer (*p*H 6·9) with 0·2% merthiolate, and 2·5 ml. of distilled water.

The authors report that R.P.R. antigens prepared by this method were stable for at least 8 months at refrigerator temperatures and for lesser periods at room temperature or at 37° C. In tests in parallel with standard R.P.R. antigen, suspensions so prepared were found to be only slightly less reactive. The omission of sodium chloride from the suspending fluid gave a finer dispersion of particles with non-reactive specimens.

A. E. Wilkinson

932. **Syphilis in Turkey.** (Syphilis in der Türkei)
A. LÜTFÜ TAT. *Hautarzt* [*Hautarzt*] **11**, 507–510, Nov., 1960. 1 fig., 5 refs.

This paper from the University Dermatological Clinic, Ankara, reviews the history of syphilis in Turkey, describes the measures taken to combat it, and discusses the incidence of the disease during the past two decades. The disease is said to have been brought to Turkey by the Jews in the 16th century, but its incidence remained low until the beginning of the 20th century, when there was a very marked increase. In 1925 measures to deal with syphilis were introduced on a nation-wide scale for the first time. The country was divided into regions in each of which there was a specialist in venereology and dermatology responsible to the Ministry of Health, while 4 or 5 physicians with special training in the subject were attached to each regional office. Clinics have been planned so that they are not more than one hour's travelling distance for the majority of the population, even in isolated rural areas.

As a result of these measures the incidence of syphilis has fallen during the past two decades. As in other countries the number of cases of early infectious syphilis increased during the Second World War, but the total number of cases of the disease in all stages actually fell during that period. Since 1949 there has been a steady decline in the number of recorded cases and in fact cases of early syphilis are now so rare that there is difficulty in finding enough patients for demonstration to medical students.

The author attributes this satisfactory situation to the active measures taken to combat the disease by the Ministry of Health.

R. D. Catterall

933. **Syphilis: Review of the Recent Literature, 1959–1960**
H. BEERMAN, L. NICHOLAS, I. L. SCHAMBERG, and M. S. GREENBERG. *Archives of Internal Medicine* [*Arch. intern. Med.*] **107**, 121–140, Jan., 1961. Bibliography.

934. **The Relationship of Human Genital Pleuropneumonia-like Organisms to Arthritis Complicating Urethritis**
D. K. FORD. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **3**, 395–402, Oct. [received Dec.], 1960. 25 refs.

The present study was undertaken at the University of British Columbia, Vancouver, in the hope that primary isolation of pleuropneumonia-like organisms (PPLO) from the joint fluid of patients with Reiter's disease might be achieved by means of human amnion tissue culture instead of directly with agar media. A total of 15 synovial exudates from 12 patients with arthritis and urethritis failed to show PPLO by the tissue-culture method, nor was any cytopathogenic change seen in the amnion preparations. In addition, 240 patients, men and women, attending a venereal disease clinic with a variety of urogenital conditions were investigated by this method. From these cases 75 strains of PPLO were isolated, but no evidence was obtainable that PPLO were aetiologically related to non-gonococcal urethritis or Reiter's syndrome.

G. W. Csonka

Tropical Medicine

935. **Screening of Cesticidal Compounds on a Tapeworm *Hymenolepis nana in vitro***
A. B. SEN and F. HAWKING. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **15**, 436–439, Sept., 1960. 10 refs.

A simple and convenient *in vitro* technique is described for the screening of compounds for action against *Hymenolepis nana* and probably many other intestinal worms. The results obtained from this test are in broad agreement with the findings of clinical experience and of a small series of *in vivo* tests. Among the substances tested, the most active ones were oil of chenopodium, dichlorophen, extract of cashew nut (*Anacardium occidentale*), antimony potassium tartrate, and BIQ 20 [eicosamethylenebis(*iso*quinolinium iodide)].—[Authors' summary.]

936. **The Treatment of Ancylostomiasis with Bephenium Hydroxynaphthoate.** (Traitement de l'ankylostomose par l'hydroxynaphtoate de béphénium)
R. CAVIER and R. BELLOW. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **53**, 623–626, July–Aug. [received Dec.], 1960. 9 refs.

The authors, working in Guadeloupe, French West Indies, confirm the opinion of previous workers regarding the advantages and efficacy of bephenium hydroxynaphthoate ("alcopar") in the treatment of ancylostomiasis. They have found that two single doses of 2·5 g. of the base given at 3 weeks' interval cured 88·4% of cases and that the drug was readily taken and produced no side-effects. It is therefore to be considered as the best drug so far produced for this purpose, that is, the elimination of *Necator americanus*.

[In their Table I, however, it is erroneously stated that in the published series by Nagaty and Rifaat and by Ahmad and Rasool cited by the authors the worm concerned was *Ancylostoma caninum*; it was in fact *A. duodenale*.] *Clement C. Chesterman*

937. **Trials of 5:5′-dichloro-2:2′-dihydroxydiphenylmethane in the Treatment of Taeniasis in Man.** (Essais de traitement du téniasis humain par le 5,5′-dichloro-2,2′-dihydroxydiphénylméthane)
J. GUILHON, M. GRABER, and A. GELLER. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **53**, 697–703, July–Aug. [received Dec.], 1960. 12 refs.

The authors report from Fort Lamy, Territory of Chad, French Africa, the treatment of 79 cases of infection with *Taenia saginata* by means of a single dose of 4·5 g. of dichlorophen, a dosage equivalent to 55 to 75 mg. per kg. body weight. They found that toxicity was less than with other known anthelminthics and that children tolerated doses of 60 to 70 mg. per kg. quite well. The drug is best given on an empty stomach and followed an hour later by a saline purge. Although they used a flavoured aqueous suspension prepared by themselves, they consider that the drug, because of its disagreeable odour, would be best given in capsules. The treatment was effective in all but 3 cases.

[The authors thus confirm the earlier work of Jackson in South Africa and the various reports by Seaton who showed that the drug is a safe and effective taenicide and should be useful in mass campaigns. They also cite the recent study by Jopling and Woodruff (*Brit. med. J.*, 1959, **2**, 542; *Abstr. Wld Med.*, 1960, **27**, 362), but these authors were using extract of male fern and mepacrine.] *Clement C. Chesterman*

938. **Synergism between Antimony (Tartar Emetic) and Thioxanthone Compounds in the Treatment of Schistosomiasis**
H. F. NAGATY, M. A. FIFAAT, and A. W. EL BOROLOSSY. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **63**, 199–203, Sept., 1960. 17 refs.

The authors of this paper from the University of Ain-Shams, Cairo, review the literature on lucanthone hydrochloride in the oral treatment of infections due to *Schistosoma haematobium* and describe clinical trials of the drug or its azathoxanthone analogue, 1-β-diethylamino - ethylamine - 4:6:8 - trimethyl - 5 - azathioxanthone, alone or in combination with tartar emetic, in patients with urinary schistosomiasis. Administration of lucanthone alone in a dosage of 10 mg. per kg. body weight daily for 12 days resulted in cure in 4 out of 10 patients assessed 120 days after treatment. Of 18 patients given tartar emetic alone in a daily dosage of 1 mg. per kg. (half the usual dose) for 12 days, 9 were cured. When these two drugs were given together in these same dosages 20 out of 21 patients were cured. There was a significant increase in the cure rate when the dosage of lucanthone given alone was doubled over a period of 10 or 12 days.

In clinical trials of the azathioxanthone analogue alone or in combination with tartar emetic a similar additive effect was observed, but unfortunately the follow-up period was not extended beyond 12 days, compared with 120 days for the lucanthone. [Thus, although the azathioxanthone–tartar-emetic combination appears to be superior, strict comparison was not possible. The advantages of combined therapy are the reduction in side-effects and in the duration of treatment to 12 days instead of more than twice this period as in the classic tartar-emetic course. Such considerations are of great importance in overcrowded hospitals, but the inclusion of intravenous injections of tartar emetic removes the outstanding advantage of oral treatment with lucanthone under less controlled conditions.] *O. D. Standen*

Allergy

939. **Formation and Destruction of C^{14} Histamine in Human Lung Tissue *in vitro***
B. LILJA, S. E. LINDELL, and T. SALDEEN. *Journal of Allergy* [*J. Allergy*] **31**, 492–496, Nov.–Dec., 1960. 15 refs.

The authors, from the University of Lund, Sweden, report the results of experiments *in vitro* designed to study the formation and catabolism of histamine in lung tissue. They found that when histidine labelled with radioactive carbon (^{14}C) was incubated with minced human lung tissue from non-asthmatic subjects and non-radioactive histamine added, very small amounts of radioactive histamine (from 2 to 15 mμg. of histamine per g. of tissue) were formed. When ^{14}C-labelled histamine was incubated with minced lung it was metabolized, the main metabolite being methylhistamine (1-methyl-4-[β-aminoethyl]imidazole).

H. Herxheimer

940. **The Separation of Substances in Timothy Pollen Extract Producing Allergic Skin Reactions from those Producing Hemagglutination Reactions**
A. MALLEY, A. LIETZE, and C. E. REED. *Journal of Allergy* [*J. Allergy*] **31**, 413–420, Sept.–Oct., 1960. 2 refs.

The haemagglutination by the serum of patients sensitive to timothy pollen of rabbit erythrocytes coupled by diazo bonds to various fractions of timothy pollen extract was studied at the University of Oregon Medical School, Portland. The pollen extract was fractionated by means of ammonium sulphate solutions. It was found that erythrocytes coupled to a fraction precipitated by a 20% saturated ammonium sulphate solution were agglutinated by the serum, but this fraction gave very weak skin reactions. Erythrocytes coupled to a fraction soluble in 49% ammonium sulphate but precipitated by a 55% solution gave low agglutination titres, but this fraction gave strongly positive skin reactions. Passive transfer tests with these fractions indicated that the haemagglutination factor is distinct from the skin-sensitizing factor and from the blocking antibody. It is suggested that the antigen and the reagin of timothy pollen are not involved in the haemagglutination reaction. *H. Herxheimer*

941. **The Reproducibility of Intradermal Skin Tests: a Controlled Study**
P. M. GOTTLIEB, S. STUPNIKER, and S. I. ASKOVITZ. *Annals of Allergy* [*Ann. Allergy*] **18**, 949–960, Sept. [received Nov.], 1960. 22 refs.

The reproducibility of the reaction to the intradermal injection of a number of allergens was studied at the Albert Einstein Medical Center, Philadelphia, in 33 patients known to be suffering from various allergic states. Six different allergens were tested on both arms on 63 occasions. It was found that the results of repeated tests differed in 13% of patients when a weal 5 mm. in diameter was considered to indicate a positive reaction. When, however, the level of discrimination was raised to 10 mm. there was complete uniformity. The tests were then repeated after an interval of about 6 months, when a discrepancy of 27% was observed with 5-mm. weals, but one of only 5% with 10-mm. weals. It is emphasized that such comparatively uniform results in subsequent tests can be obtained only if the same technique is scrupulously maintained. Tests should be read between 10 and 15 minutes after the injection and only weals 10 mm. or more in diameter should be considered to indicate a positive reaction. *H. Herxheimer*

942. **Cardiac Asthma—a Misnomer**
L. TUFT and L. S. GIRSH. *Journal of Allergy* [*J. Allergy*] **31**, 519–530, Nov.–Dec., 1960. 10 refs.

In an attempt to determine whether so-called cardiac asthma exists as a separate entity the authors, at Temple University Medical Center, Philadelphia, have reviewed the records of 103 cases of bronchial asthma with co-existent cardiovascular disease, some of which had actually been given the diagnosis of cardiac asthma. The clinical features in these cases were compared with those in 109 control cases of either hypertension or coronary arterial disease. Only one case in the first group had the typical symptoms of cardiac asthma, and there was only one patient with typical wheezing in the control group. The authors point out that cardiac disease and bronchial asthma often occur together, and that such patients usually benefit from anti-asthmatic treatment given at the same time as that for the heart condition. They suggest that typical cardiac asthma is rare and that the condition does not deserve this designation, because the wheezing, though caused by left ventricular failure, originates in the bronchi. They therefore recommend that the term " cardiac asthma " be abandoned.

[No doubt the diagnosis of cardiac asthma is often made without sufficient reason. The authors of this interesting study seem to neglect, however, the symptom of cough, which is decisive in the differential diagnosis. In cardiac asthma cough is either absent or confined to the end of the nocturnal attack, while in cases of bronchial asthma of cardiac origin cough is a frequent occurrence.] *H. Herxheimer*

943. **A Comparison of the Growth Suppressive Effect of Cortisone, Prednisone, and Other Adrenal Cortical Hormones**
T. E. VAN METRE JR., W. A. NIERMANN, and L. J. ROSEN. *Journal of Allergy* [*J. Allergy*] **31**, 531–542, Nov.–Dec., 1960. 5 figs., 19 refs.

A study was carried out at the Johns Hopkins Hospital, Baltimore, Maryland, to compare the growth-inhibiting effects of prolonged treatment with corticosteroids in children with intractable bronchial asthma. In most of

the 19 cases studied the asthma had started in the first 2 years of life; treatment was with maintenance doses of various corticosteroid preparations. In every case the steroid drug was frequently changed and there were intervals when none was given. Linear growth and weight gain were plotted against the normal development. It was found that cortisone did not impair normal linear growth, whereas most of the other steroids did. [The accompanying table shows that linear growth was completely suppressed in only 6 instances, in 5 of which the corticosteroid was given for periods as short as one to 4 months; there are 11 other examples in which less than 50% of normal linear growth occurred, but here also the period of observation was often not long enough to exclude a natural temporary interruption of linear growth, as is often seen in children. The cortisone- and corticosteroid-free periods, however, are much longer, and therefore do not contain this element of error. The evidence for the growth-suppressive effect of prednisone and other corticosteroid preparations will, in the circumstances, require strengthening.]

H. Herxheimer

944. **Treatment of Asthma by Subcutaneous Injection of a Gamma-globulin and Histamine Complex.** (Traitement de l'asthme par des injections sous-cutanées d'un complexe de gamma-globuline et d'histamine)
G. MORICHAU-BEAUCHANT and —. DAJEAN. *Presse médicale* [*Presse méd.*] **68**, 1512–1514, Sept. 24, 1960. 27 refs.

Since 1947 it has been known that the injection of 2 ml. of normal human serum into guinea-pigs protects these animals from the effects of a lethal dose of histamine aerosol, whereas the serum of an asthmatic person does not. The treatment in this way of asthmatic patients with the most powerful human sera available resulted in improvement in two-thirds of them. Later on, in 1958, the results were still further improved by adding gamma globulin to the therapeutic sera; this substance induces the formation of antibodies equal to those of healthy persons, with the difference, however, that they are transitory and must be restored by a repetition of the treatment. As the formation of antibodies takes time this treatment cannot be used in cases of acute asthmatic attacks or paroxysms. Further, it does not eliminate the conflict between antibodies and antigens caused by allergenic agents to which the patient is sensitive, but it does prevent the harmful results of liberated histamine, such as oedema, vasodilatation, and bronchial spasm.

In the present study, from which only patients with emphysema and those in whom the allergenic agent was not known for certain were excluded, the treatment consisted in giving three subcutaneous injections each of 2 ml. of a gamma-globulin–histamine complex at intervals of 4 days. Of 33 patients so treated, 3 showed excellent results (no attacks for at least 4 months), 16 had good results (no attacks, but sometimes slight oppression), while in a further 7 cases the results were mediocre (temporary improvement, but with definite recurrences); in the remaining 7 the treatment was a failure. In some cases a good result was evident as early as the day after the first injection but, as the authors point out, this rapid improvement, or conversely some failures, cannot be taken at their face value because of other, psychosomatic, factors involved. On the other hand there was in some cases recrudescence of attacks during a period of weeks, but by treatment with antihistaminics and theophylline, avoiding corticoids and sympathomimetic drugs, a consolidated improvement lasting from 4 to 6 months or more could rapidly be obtained. After this time retreatment with the initial dosage frequently gave good results and is recommended as a routine measure. The authors state that the treatment described is harmless and may be given to young children without danger.

Robert E. Lister

945. **Treatment of Hypersensitiveness to Iodized Roentgen Contrast Media.** [In English]
B. ARNER. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 432–441, 1960. 1 ref.

Following upon the injection of iodized contrast media allergic symptoms such as urticaria, sneezing, or asthma may occur. These are usually mild, but may sometimes be severe. Since it may be necessary to carry out further radiological investigation after such a reaction some form of test for the existence of allergy to iodine compounds would be useful, but it is agreed that skin tests and conjunctival tests are of no value in this connexion. It is suggested that the addition of antihistaminic drugs to contrast media might prevent the development of mild allergic symptoms. The cases of 5 patients (3 under treatment at the Serafimer Hospital, Stockholm, and 2 at the University Renal Clinic, Lund, Sweden) who had previously reacted to the injection of contrast media and whose condition required repeated radiological examination are described. In each case it was found that tolerance to the contrast medium could be increased by injecting the preparation, diluted 100 times, first subcutaneously and then intravenously in increasing doses, about 20 injections being spaced out at 2-hourly intervals over a period of 4 days. It is stressed that hyposensitization induced in this way should be regarded as only temporary and that the x-ray examination should be carried out immediately the treatment is concluded.

A. W. Frankland

946. **Occurrence of Allergic Rhinitis among Schoolchildren.** [In English]
I. ENGSTRÖM, S. KRAEPELIEN, and K. LINNEROTH-ELZVIK. *Acta allergologica* [*Acta allerg.* (*Kbh*)] **15**, 459–465, 1960. 1 fig., 13 refs.

The 6,714 replies to a questionary sent to the parents of 6,876 elementary school-children in Stockholm showed that 98, or 1·5%, suffered from seasonal allergic rhinitis (hay-fever). The addition of 21 cases of other, non-seasonal, allergic rhinitis gave a total incidence of 1·8%. Three-quarters of all cases occurred in boys, and in one-third of cases the onset was before the age of 4. Seasonal hay-fever is more common in the suburbs, and it is suggested that this is due to the greater possibilities for sensitization in these less urbanized areas.

A. W. Frankland

Nutrition and Metabolism

947. **The Case for Euthyroid Hypometabolism**
M. GOLDBERG. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 479–493, Oct., 1960. Bibliography.

After a brief review of the evidence for and against the existence of the syndrome of "euthyroid hypometabolism" the author reports from the Allied Powers' Headquarters (SHAPE), Paris, that among some 500 patients, military personnel and their dependants, referred on account of psychoneurotic symptoms he found 32 who fulfilled the diagnostic criteria, that is, a symptom complex comprising hypometabolism and psychoneurosis, normal thyroid function (as shown by a normal serum protein-bound iodine level and a normal rise in this level after the administration of thyroid-stimulating hormone), a low basal metabolic rate (B.M.R.), prolongation of the ankle-jerk reflex time, no response to placebos, and little or no response to thyroid extract but a good, sustained response to L-triiodothyronine (T-3). All the patients were followed up for a minimum of 5 months and the B.M.R. serially determined, the author having found that in such cases the first reading is often falsely normal. The tendon reflex time was measured electrically, this factor being in the author's experience a more reliable guide to the syndrome than the B.M.R.

The effective dose range of T-3 was 75 to 150 (mean 112) μg.; paradoxically, in some patients given 12 to 60 μg. there was an increase in symptoms, this presumably being due to suppression of endogenous thyroid hormones. With the dosage of 75 to 150 μg., which was found to be safe and to cause no side-effects, 23 of the 32 patients became asymptomatic on this treatment alone. In some cases tranquillizing drugs appeared to reduce the effectiveness of T-3, probably, it is suggested, because they block the peripheral action of thyroid hormones. Consequently all patients should be weaned from such drugs before treatment with T-3 is instituted. In 3 patients there was evidence of adrenocortical dysfunction as manifested by low total urinary 17-ketosteroid excretion, this value increasing after treatment with T-3. Of 9 patients subjected to glucose tolerance tests, a flat curve was found in 4. One patient with anorexia nervosa following pregnancy, who also appeared to have the hypometabolic syndrome, responded to treatment with T-3; the case history of this patient is presented and the literature on the syndrome reviewed.

Expressing his belief that the euthyroid hypometabolic state exists as a distinct entity of unknown aetiology, the author suggests that it may result from the depletion of T-3, but not of thyroxine, in the thyroid gland as the result of long-continued stress, which according to some authorities increases the output of thyroidal thyroxine and T-3 by way of an excess of adrenal medullary hormones. He also notes that neurosis may pre-exist and may be the cause of the hypometabolic state : he recommends that the tendon reflexes of all psychoneurotic patients should be carefully examined and timed.

A. Gordon Beckett

948. **The Chemical Diagnosis of Steatorrhoea**
E. B. HENDRY. *British Medical Journal* [*Brit. med. J.*] **2**, 975–979, Oct. 1, 1960. 12 refs.

At the Western Infirmary, Glasgow, the percentage of fat in the dried faeces and the daily fat excretion were determined in 231 fat-balance studies lasting 3 to 7 days on 138 patients suspected of steatorrhoea who received 70 to 75 g. of fat daily. The balances were repeated in 66 cases, with fair or good agreement in 55 (83%). The relationship between daily fat excretion and the percentage of fat in dried faeces was analysed, it being assumed that a daily output of 5 g. or more and a faecal fat content of 25% or more were abnormal and indicative of steatorrhoea.

It was found that the daily fat excretion was a better index of steatorrhoea than the percentage of fat in the faeces, the latter being influenced by the non-fatty residues of the diet; it is suggested that in interpreting figures for faecal fat content the dry weight of the faeces should be taken into consideration. As a screening test, however, the author regards a faecal fat content of less than 10% of the dry weight in a single 24-hour specimen as excluding steatorrhoea.

M. Lubran

949. **The Treatment of Obesity by the "High-fat" Diet. The Inevitability of Calories**
J. YUDKIN and M. CAREY. *Lancet* [*Lancet*] **2**, 939–941, Oct. 29, 1960. 14 refs.

In the last few years various investigators have reported that a satisfactory reduction of the weight of obese patients can be obtained without causing hunger by giving diets in which only the carbohydrate content is reduced. Since these diets allow unrestricted amounts of protein and fat, they are sometimes referred to as "high-fat" rather than "low-carbohydrate" diets. In seeking to explain this somewhat unexpected loss of weight some investigators have suggested that obese patients alter their metabolism in response to this diet. This view has been contested, however, by the senior author of the present paper from Queen Elizabeth College and St. George's Hospital, London, who believes that the diet leads to a loss of weight because, in spite of its unrestricted allowance of fat and protein, it is in fact a low-calorie diet.

Investigations were carried out on 6 adults, of whom 4 were nursing sisters; apart from being overweight, all were apparently healthy and were working during the time of the investigations. They were instructed to eat their usual foods for 2 weeks and then to reduce their carbohydrate intake to about 50 g. daily, taking as much protein and fat as they liked, for a further period of 2

weeks. They were instructed in the weighing and recording of their dietary intake and weighed themselves daily at the same time of day throughout the 4 weeks of the study.

The intake of calories, protein, fat, and carbohydrate was calculated from the daily dietary records. The caloric intake in all subjects fell significantly during the period of the low-carbohydrate diet, the reduction ranging from 200 to 1,900 Calories or from 13% to 55% daily. In all cases the normal intake of carbohydrate was substantially reduced, daily averages of between 140 and 500 g. approximately being reduced to between 30 and 55 g. No subject consumed significantly more fat than in the control period, while in 3 cases there was a significant reduction in the intake of fat. The protein intake was not affected by the change in diet. All 6 subjects lost weight during the 2 weeks on the low-carbohydrate diet; 5 lost between 5 lb. (2·3 kg.) and 9 lb. (4·1 kg.) and the remaining subject lost 2 lb. (0·9 kg.). None of the subjects complained of hunger.

Thus, for practical purposes, when the dietary allowance of fat is unrestricted fat intake turns out to be no greater than before, sometimes even less. Therefore the term " high-fat diet " is a misnomer and the correct term is " low-carbohydrate diet ", the loss of weight being due to a reduction in caloric content. The implications of these findings are discussed in relation to theories of appetite control. *Joseph Parness*

950. **A Special Form of Hypokalaemia: Psychogenic Depletion Due to the Abuse of Laxatives.** (Une forme spéciale d'hypokaliémie: la dénutrition psychogène par abus de laxatifs)
C. PERRIER. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **5**, 792–807, Oct., 1960. 7 figs., bibliography.

Potassium depletion due to excessive purgation was the common factor in the 4 cases here described from the University Therapeutic Clinic, Geneva. The 3 female patients, aged 31, 43, and 29 respectively, showed psychological abnormalities; the fourth patient was a man aged 76. Each case is reported in detail, together with the tabulated results of electrolyte and metabolic and balance studies; in addition a description is given of the results of experimental potassium depletion in a healthy woman aged 34. In 3 of the author's patients a history of anorexia was obtained, while the fourth had restricted her diet and induced vomiting after meals. Laxatives had been used to excess by all 4 for many years. One woman had had cyclic oedema, the other 2 women reported intermittent swelling of the ankles, and the man presented with gross oedema. All were weak, 2 of the women had had tetany, and 2 complained of persistent thirst. Initial serum potassium concentrations were between 1·7 and 3·3 mEq. per litre and the urinary excretion of potassium was low in all. Sodium loads were not excreted. Potassium replacement, which was accompanied by remission of the physical symptoms and signs, was achieved by means of oral and intravenous supplements of potassium chloride or citrate; these indicated that the deficit of potassium was of the order of 400 to 700 mEq. Potassium retention was accompanied by sodium loss.

Other reports in the literature of potassium depletion due to loss of potassium in the stools are reviewed. The long discussion which follows is concerned principally with the oedema, disorders of renal and gastro-intestinal function, and tetany which variously result from potassium depletion, but also includes the psychological factors involved in these patients, in the treatment of which simple psychotherapy is often helpful.

G. C. R. Morris

951. **Siderosis in the Bantu: a Combined Histopathological and Chemical Study**
T. H. BOTHWELL and B. A. BRADLOW. *Archives of Pathology* [*Arch. Path.*] **70**, 279–292, Sept., 1960. 23 refs.

At the University of Witwatersrand Medical School, Johannesburg, specimens of the liver of 147 Bantu subjects aged 11 to 70 years (131 of them males) who had died traumatic deaths were studied both histologically and chemically. In 131 cases (89%) the concentration of iron (given as per cent. dry weight) was above the accepted upper limit of normal (0·1%). Although the results showed a wide scatter, there was a tendency for the concentration to rise with age, the maximum concentrations being found in the age group 40–50 years. About half those with a relatively small concentration of iron (up to 0·6%) showed histologically an increase of iron content in the parenchymal cells and less than one-fifth in the Kupffer cells, whereas all those with the higher concentrations (that is, above 2%) showed heavy deposits of iron visible in the parenchymal cells, the Kupffer cells, and the portal tracts. In 5 of the 96 specimens with iron concentrations below 0·5% and 8 of the 40 with concentrations between 0·5 and 1% there was mild portal fibrosis, whereas all of the 11 with concentrations above 2% showed moderate or severe fibrosis. Cellular infiltration in the portal tracts was noted in 60 cases, mild fatty infiltration in 7, and acute hepatitis in one. A close correlation was found between the iron concentration in the liver and that in the spleen, specimens of which were available in 50 cases.

The increased deposit of iron in the liver is thought to be related to the high daily intake of iron by the Bantu, often over 100 mg. per day, resulting in blood iron levels twice as high as those in normal white males. The high intake also leads to an impairment of the release of iron from the spleen and other reticulo-endothelial tissue and hence to a gradual accumulation of iron derived from breakdown of these tissues. Some of the iron in the portal tract may come from the breakdown of iron-laden parenchymal cells. Although the basic foodstuffs of Bantus, such as maize, contain a considerable amount of iron, it is considered that most of the excess iron is derived from the iron utensils used in cooking and in the preparation of fermented beverages. The cause of the excessive absorption of iron from the alimentary tract is not known, although it may be due to some metabolic deficiency associated with malnutrition. The close correlation between the presence of gross excess of iron in the liver and that of fibrosis or cirrhosis suggests a direct causation. *A. Gordon Beckett*

Gastroenterology

952. **Carcinoma and Ulcerative Colitis: Prognosis**
J. A. BARGEN and R. P. GAGE. *Gastroenterology* [*Gastroenterology*] **39**, 385–393, Oct., 1960. 3 figs., 19 refs.

A survey of the records of 7,000 patients with ulcerative colitis seen between 1913 and 1958 at the Mayo Clinic showed that there were 178 (100 men and 78 women) with complicating carcinoma of the large intestine. In over 75% of these cases (136) symptoms of colitis appeared before the age of 40, while in 33 the carcinoma, often highly malignant, was diagnosed when the patient was under the age of 30; the mean interval between the onset of colitic symptoms and the diagnosis of carcinoma was 17 years, the great majority lying within the range of 10 to 24 years. Just over one-quarter of the tumours (47) arose in the rectum, about another quarter (43) originated at multiple locations, and nearly one-half (80) were distributed equally between the caecum, transverse colon, and sigmoid; in 8 cases the site was not stated. In only 64 patients was there pseudopolyposis, but in 27 secondary adenomatous polyposis developed later. The probable survival rate (calculated actuarily) was 46%, while the actual survival rate was 48·8% over the whole period. This figure compares favourably with the survival rate in patients with cancer of the colon not complicated by ulcerative colitis.

The authors recommend regular proctoscopic and radiological examination (every 6 to 12 months) of patients with advanced and long-standing ulcerative colitis, total colectomy to be performed when carcinoma is diagnosed. They do not recommend this operation as a prophylactic measure since the long-term risks of colectomy and ileostomy are not precisely known and " may well be greater than the risk that carcinoma will develop." *Arnold Pines*

953. **An Assessment of Prednisone, Salazopyrin, and Topical Hydrocortisone Hemisuccinate Used as Outpatient Treatment for Ulcerative Colitis**
J. E. LENNARD-JONES, A. J. LONGMORE, A. C. NEWELL, C. W. E. WILSON, and F. AVERY JONES. *Gut* [*Gut*] **1**, 217–222, Sept., 1960. 2 figs., 10 refs.

Two trials of prednisone, " salazopyrin " (sulphasalazine), and topical hydrocortisone in the treatment of mild active ulcerative colitis were carried out in the out-patient clinic at St. Mark's Hospital, London. In the first trial (19 patients) prednisone gave significantly better results (remission in 13, improvement in 4 patients) than a placebo (remission in 3 and improvement in 3). In the second trial (20 patients in each subgroup) the efficacy of sulphasalazine (remission in 8 and improvement in 5) was found to be intermediate between that of prednisone (remission in 11 and improvement in 4) and that of topical hydrocortisone (remission in 3 and improvement in 5), although the differences between the results obtained with all three drugs and the placebo were not statistically significant. Sulphasalazine produced remission more slowly than did prednisone.

There were no serious side-effects of steroid therapy, but 12 of the patients given sulphasalazine complained of unpleasant reactions, including nausea (4), anorexia (3), vomiting (2), malaise (2), diarrhoea (1), and skin rash (1). Of the 33 patients in remission after treatment with prednisone, 19 relapsed during the following 6 months (follow-up data incomplete in 2), and of the 12 patients in remission at 6 months, 4 relapsed during the next 6 months. The numbers in remission in the other groups were too small to permit valid conclusions about the relapse rate.

The disappointing results obtained with topical hydrocortisone are attributed to the " technique of administration which was not suitable for ordinary out-patient use ". *A. Gordon Beckett*

954. **Retroperitoneal Fibrosis: an Anatomic and Radiologic Review with a Report of Four New Cases and an Explanation of Pathogenesis**
J. DINEEN, T. ASCH, and J. M. PEARCE. *Radiology* [*Radiology*] **75**, 380–390, Sept., 1960. 14 figs., 30 refs.

The authors of this paper from the New York Hospital–Cornell Medical Center, New York, report 4 cases of benign idiopathic retroperitoneal fibrosis. The aetiology of this rare condition is discussed and the clinical features are described. The latter consist of months of ill-health, vague abdominal pain, loss of weight, and pain in the flank often with a testicular component. Occasionally complete anuria is the presenting feature. The disease is bilateral in the majority of cases. Physical examination is unrewarding and a palpable mass uncommon. The radiological appearances are not specific, being those of hydronephrosis; the proximal ureter is dilated and tortuous, and the ureter tapers gradually to a fixed stenotic segment varying from 3 to 6 cm. in length opposite the bodies of the 4th and 5th lumbar vertebrae. Normal ureteral calibre is then gradually resumed. In one of the patients there were numerous small sacculations in the region of the involvement. The histological appearances of the disease are those of a sclerosing lipogranuloma.

The authors emphasize the benign nature of the disease and the need for early surgery. They consider the treatment of choice is early ureteral lysis and transplantation, with or without nephrostomy. *I. McLean Baird*

955. **Apoplexy of the Lesser Omentum**
L. PELNER and N. MITCHELL. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 634–638, Nov., 1960. 2 figs., 6 refs.

Lesions of the lesser omentum appear to be exceedingly rare, but in this paper from New York State University Medical Center and the Swedish Hospital,

Brooklyn, the authors describe 2 cases of apoplexy of this tissue seen in recent years. So far as they could ascertain no exactly similar cases of this condition have previously been described in the literature. The lesion consisted of a localized haemorrhage in the small omentum near the lesser curvature of the stomach, with early spindle-shaped fibroblastic proliferation accompanied by small capillary formations. There was no venous thrombosis and no evidence of necrosis of the vascular walls. Both the patients were women, aged 45 and 49 years respectively. Clinically, the main features were a sudden onset of severe abdominal pain in the epigastrium or right upper quadrant, without vomiting, heartburn, or belching, followed by difficulty in straightening up and walking. There was abdominal tenderness in the region of the pain and a mild pyrexia for a few days. There was no history of injury in either patient. In each case a diagnosis of perforated gastric ulcer was made and subtotal gastrectomy performed. Only postoperatively, when the resected portion of the stomach and adherent tissues could be thoroughly examined, did the true diagnosis come to light. The difficulty of making a definite preoperative diagnosis of this rare condition is discussed. In discussion of the pathogenesis it is postulated that a sudden increase in intra-abdominal pressure, as in coughing or sneezing, might be sufficient to cause haemorrhagic extravasation. *M. Lubran*

STOMACH AND DUODENUM

956. **Gastric Atrophy, Atrophic Gastritis, and Gastric Secretory Failure. Correlative Study by Suction Biopsy and Exfoliative Cytology of Gastric Mucosa, Paper Electrophoretic and Secretory Assays of Gastric Secretion, and Measurements of Intestinal Absorption and Blood Levels of Vitamin B_{12}**
G. B. J. Glass, F. D. Speer, H. E. Nieburgs, A. Ishimori, E. L. Jones, H. Baker, S. A. Schwartz, and R. Smith. *Gastroenterology* [*Gastroenterology*] **39**, 429–453, Oct., 1960. 11 figs., bibliography.

The relative importance, usefulness, and accuracy of various techniques employed in the diagnosis of gastric atrophy were studied in 187 patients over 52 years of age, including 112 with histamine-fast achlorhydria. With Wood's tube gastric biopsy specimens were successfully obtained in 83·5% of cases, the histological findings being then classified as normal, gastritis without atrophy, gastritis with slight atrophy, advanced atrophic gastritis, or gastric atrophy. Using Nieburgs' technique for exfoliative cytology and a modified Papanicolaou stain, the authors distinguished by their nuclei five types of epithelial cell, which corresponded well with the biopsy findings. From the results of gastric secretion studies secretory failure was classified as mild, moderate, advanced, or complete. Mild and moderate failure were associated with gastritis and, in a few instances, with slight to advanced atrophy; advanced failure was almost always associated with advanced atrophic gastritis and complete failure with complete atrophy or advanced atrophic gastritis. A simplified double histamine test was found as useful as more elaborate tests of acid secretion. A positive result with the azure A (" diagnex ") urinary test indicated the presence of free hydrochloric acid in the stomach, but a negative result was inconclusive. Three electrophoretic patterns of gastric juice were recognized: (1) normal, associated with normal or gastritic mucosa; (2) " incomplete ", associated with gastritis and slight or advanced atrophy; and (3) " compressed ", which was pathognomonic of advanced atrophy. Paper electrophoresis was also useful in detecting massive leakage of serum albumin into the gastric lumen. Abolition of intestinal absorption of radioactive vitamin B_{12} (cyanocobalamin), which could be corrected by administration of intrinsic factor, was observed in pernicious anaemia after subtotal gastrectomy and also in 12 patients with mild or advanced gastric secretory failure not associated with signs of pernicious anaemia, in 5 of whom biopsy specimens showed advanced mucosal atrophy. The blood level of vitamin B_{12} was low in most patients with pernicious anaemia and also in several patients with histamine-fast anacidity and mucosal atrophy but an adequate secretion of intrinsic factor; it is suggested that in the latter group atrophy is the result rather than the cause of the vitamin deficiency. *A. Wynn Williams*

957. **Experimental and Clinical Considerations on Hesperidin–Ascorbic Acid in Upper Gastrointestinal Bleeding**
T. Bodi and B. Weiss. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 402–413, Oct., 1960. 16 refs.

Quoting previous observations that vitamin C (ascorbic acid) and bioflavonoids have proved beneficial in the treatment of peptic ulcer, the authors report that in 3 out of 5 patients with peptic ulcer seen at Jefferson Medical College Hospital, Philadelphia, in whom gastric bleeding was induced by histamine–insulin stimulation the administration of capsules containing 100 mg. of hesperidin together with tablets containing 200 mg. of ascorbic acid two or three times a day reduced the amount of bleeding compared with that in a pre-treatment period. A further 11 patients with peptic ulcer and gastro-duodenal haemorrhage who were then treated in the same way, in addition to receiving standard treatment with diet and antacids, also appeared to benefit. The authors postulate that patients with a bleeding ulcer may be deficient in vitamin C and that hesperidin methylchalcone may inhibit release of histamine from the blood cells. Individual results are tabulated and selected case histories described. *Thomas Hunt*

958. **The Dual Role of the Adrenal Glands in the Pathogenesis of Peptic Ulcer**
E. E. Woldman, D. Fishman, and A. J. Segal. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 390–396, Oct., 1960. 1 fig., 11 refs.

In order to throw further light on the apparent paradox that both hypoadrenalism and hyperadrenalism are associated with the development of peptic ulcer the authors report the findings in 1,102 necropsies performed at St. Luke's Hospital, Cleveland, Ohio, in

which the condition of the adrenal glands was specially examined in relation to the incidence of focal mucosal haemorrhages, haemorrhagic erosions, and acute ulcers in the subject's oesophagus, stomach, and duodenum, care being taken to exclude lesions due to post-mortem changes. The pathological findings in the adrenal glands were graded as either mild or severe, the former including merely congestion and round-cell infiltration and the latter such changes as haemorrhage, necrosis, atrophy, fibrosis, or neoplastic metastases. The mucosal lesions in the stomach and duodenum were mostly close to the surface, and similar lesions also occurred in the jejunum, ileum, and colon; the largest mucosal haemorrhages were about 3 cm. in diameter.

It was noted that of the 181 cases in which severe adrenal changes were found, 84 (46%) showed either acute peptic ulcer or focal haemorrhage, whereas of 439 cases in which no microscopic abnormalities were found in the adrenal glands, only 84 (19%) showed changes in the stomach or duodenum, while such changes were present in 27% of cases showing mild adrenal abnormalities. This apparent correlation is attributed by the authors to a dual role of adrenal gland activity. They suggest that adrenal cortical insufficiency (hypocorticism), perhaps as a result of a stressful situation, initiates an acute lesion in the stomach or duodenum such as may also occur following suppression of adrenocortical function after prolonged administration of exogenous corticosteroids. This short period of lessened activity may be followed by hypercorticoid activity, which stimulates gastric hypersecretion and at the same time suppresses inflammatory and repair processes. It is this stage which the authors regard as being the starting point of chronic peptic ulcer. [This is only deduction and no evidence that such a process actually takes place is offered. Their findings that a high incidence of ulcerative lesions in the gastro-intestinal tract was associated with damage to the adrenal glands, however, confirms previous experimental work reported in the literature.] *Thomas Hunt*

959. **Prevention of Relapse in Peptic Ulcer.** (Опыт противорецидивного профилактического курса лечения язвенной болезни)
M. D. Byhovec. *Советская Медицина* [*Sovetsk. Med.*] **24**, 134–135, Oct., 1960.

In this discussion of measures to prevent relapse in peptic ulcer the author recommends that after recovery from the original attack the patient should be kept under periodic observation for 3 to 4 years until the motor and secretory activity of the stomach returns to normal. The greatest number of relapses occur in the autumn (44%) or spring (33%) and are best prevented by such measures as work resettlement with provision for the necessary amount of rest, accompanied by a regular life, regular meals, a rational diet, total abstinence from alcohol and tobacco, " medical gymnastics ", and sport activities. Courses of medical treatment designed to prevent relapse should include administration of atropine, alkalis, sodium bromide, histidine, intravenous glucose, and subcutaneous insulin.

During 1958–9 517 patients (86% of them men), mostly aged between 20 and 40, were treated by this regimen. Each patient was examined at least once every 3 months and 32 of them received 3 courses of the treatment, 321 two courses as out-patients, 101 one out-patient and one in-patient course, and 63 one out-patient course. Only 57 of the 517 patients deteriorated and such deterioration was usually associated with some stressful complication at work. In 1958 the over-all incidence of exacerbations, compared with that in 1957, was reduced by 38%. It was found that such preventive courses of treatment lasting 2 to 3 weeks given in the spring and autumn were effective in arresting the progress of the disease, preventing relapse, and reducing the incidence of complications and chronic invalidism.
S. W. Waydenfeld

LIVER AND GALL-BLADDER

960. **The Differential Value of Bromsulfalein Retention Tests in Acute Hepatitis and Obstructive Jaundice**
J. S. Reich and W. D. Davis Jr. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **5**, 770–775, Sept., 1960. 2 figs., 9 refs.

The value of the " bromsulphalein " retention test in the differential diagnosis of acute hepatitis and obstructive jaundice was studied in 101 patients (75 with infective hepatitis and 26 with extrahepatic obstructive jaundice) at the Ochsner Foundation and Charity Hospitals, New Orleans. Bromsulphalein retention was determined 45 minutes after injection of 5 mg. of the drug per kg. body weight; in patients with hepatitis this value was estimated when the jaundice was at its height. Of the 26 patients with obstructive jaundice, 21 had bromsulphalein retention of less than 50%; of the 75 with hepatitis, 56 had retention of over 50% at 45 minutes. In spite of the overlap in the results the authors consider that the bromsulphalein retention test may be of assistance in the differential diagnosis of jaundice. *P. C. Reynell*

961. **Hypokalemia in Liver Disease**
H. O. Heinemann and C. Emirgil. *Metabolism: Clinical and Experimental* [*Metabolism*] **9**, 869–879, Oct. [received Dec.], 1960. 2 figs., 33 refs.

Hypokalaemia can occur in hepatic failure in the absence of diuretic treatment and has been ascribed to deficient intake of potassium because of anorexia. Observations at the Francis Delafield Hospital, New York, on 5 patients with cirrhosis and hypokalaemia did not, however, support this view, since the patients responded promptly to changes in intake of potassium by changing their urinary potassium output, whereas patients with a true deficiency of potassium would have retained potassium when the intake was high. This evidence likewise makes an abnormal renal loss of potassium an unlikely explanation for the hypokalaemia of cirrhosis. Respiratory alkalosis, which can occur in cirrhosis, was excluded as the cause of hypokalaemia in these patients by the lack of any correlation between pCO_2 and plasma potassium level, and by failure to raise the plasma potassium level by inducing acidosis.

[No explanation for hypokalaemia is advanced; insufficient clinical information is given to show whether the ascites in these patients was ever tapped, and the possibility of loss of potassium in this way is not considered.]

D. A. K. Black

962. **Flow Rate and Composition of Thoracic-duct Lymph in Patients with Cirrhosis**

A. E. DUMONT and J. H. MULHOLLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 471–474, Sept. 8, 1960. 2 figs., 13 refs.

The authors report from Bellevue Hospital, New York, that in a study of 4 patients with Laënnec's cirrhosis due to chronic alcoholism three striking abnormalities were observed in all 4: (1) the thoracic duct was twice to 4 times as large as the normal duct and was accompanied by one or more large parallel lymphatic channels; (2) the lymph in all was grossly haemorrhagic owing to the presence of intact erythrocytes, the average haematocrit value being 6%; and (3) lymphatic flow was from 3 to 6 times the usual normal rate of 1 ml. per minute. The authors state that " although total protein concentration was less in lymph than in serum, electrophoretic studies demonstrated that the percentage of total protein present in the various fractions was the same in both fluids " [a statement not entirely supported by the figures given for the authors' 4th case]. In the first patient, who had both ascites and oesophageal varices, the average lymph flow was 6 to 7 ml. per minute and the ascites diminished during the period of drainage. In the second patient, who had oesophageal varices only, the portal pressure was initially 360 mm. H_2O and the lymph flow 3 ml. per minute; after performance of a portacaval shunt these values fell to 210 mm. H_2O and 0·3 ml. per minute respectively. In the third patient, who had ascites only, the lymph flow over 4 days averaged 4 to 6 ml. per minute; the injection of albumin labelled with ^{130}I into the ascitic fluid was followed by the rapid appearance of the protein in the thoracic-duct lymph, thus demonstrating the transport of protein from ascitic fluid to local lymphatics and thence to the duct and finally to the serum. In the 4th patient, who had neither ascites nor oesophageal varices, the lymph flow was about 2 ml. per minute during the 2 days over which it was collected.

[This paper appears to be of the nature of a preliminary communication, and the authors state that further work on the subject is in progress. The results are interesting, but as yet not very conclusive, there being so much difference clinically between the 4 patients.]

W. H. Horner Andrews

963. **Colloid Osmotic Pressure and Hydrostatic Pressure Relationships in the Formation of Ascites in Hepatic Cirrhosis**

G. R. CHERRICK, D. N. S. KERR, A. E. READ, and S. SHERLOCK. *Clinical Science* [*Clin. Sci.*] **19**, 361–375, Aug. [received Oct.], 1960. 4 figs., 39 refs.

The formation of ascitic fluid is probably in accordance with the equation for equilibrium enunciated by Starling in 1894, which may be stated as follows: plasma colloid pressure minus ascitic fluid colloid pressure equals portal capillary pressure minus abdominal hydrostatic pressure. Various authors have investigated the problem, but measurements of all the above four factors do not seem to have been made before the present study, here reported from the Postgraduate Medical School of London. The 45 patients investigated were considered in two groups: (1) 35 without ascites, nearly all of whom had liver disease, and (2) 10 patients with Laënnec's cirrhosis and ascites. In 2 patients the portal pressure was estimated from the hepatic vein wedged pressure, while in the others it was obtained from the intrasplenic pressure. Serum colloid osmotic pressure and, when present, ascitic fluid colloid pressure were measured by means of the Rowe electronic colloid osmometer.

Although the intrasplenic pressure was significantly lower in patients without ascites (mean 291 ± 73 mm. H_2O) than in those with ascites (mean 387 ± 101 mm. H_2O), the effective portal pressure, that is, intrasplenic pressure minus the hydrostatic pressure of the ascitic fluid (when present), was virtually the same in both groups. There was a clear difference between the two groups in regard to serum colloid osmotic pressure: thus, with one exception, in all patients with oedema or ascites this pressure was 270 mm. H_2O or less, whereas in all those without oedema or ascites it was over 270 mm. H_2O, there being no overlap. Moreover when the osmotic pressure of the ascitic fluid was taken into account and subtracted from the above values the difference between the two groups became even greater. The net transfer pressure, which takes into account all the forces tending to drive fluid from the portal vessels into ascitic fluid, can be expressed in patients with ascites as the sum of the intrasplenic pressure plus the ascitic fluid colloid pressure minus the sum of the serum colloid osmotic pressure and the intra-abdominal pressure; in patients without ascites the net transfer pressure is more simply the intrasplenic pressure minus the serum colloid pressure. In the patients without ascites the net transfer pressure ranged from -262 to $+116$ mm. H_2O. In 7 of this group the pressure was positive, that is, favouring the formation of ascites, but in 2 only was it over 40 mm. H_2O. In the patients with ascites, however, the net transfer pressure ranged from -12 to $+208$ mm. H_2O and in only 2 was the value less than $+40$ mm. H_2O.

W. H. Horner Andrews

964. **Cirrhosis in Young Women**

O'N. BARRETT JR. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 493–496, Nov., 1960. 16 refs.

The occurrence of cirrhosis of the liver in young adults which is not due to alcoholism or nutritional deficiency has been reported by various authors, and it has been noted that most of these cases occur in females. In some of the cases, but not all, a relationship to previous attacks of infective hepatitis has been established. In the present paper from the Walter Reed Army Medical Center, Washington, D.C., a case of cirrhosis in a white female aged 24 years is described. There was no history of infective hepatitis. The disease developed insidiously, and during 4 years it ran a progressive downhill course. By this time the patient was jaundiced, with spider angiomata over the upper thorax, bleeding from the

gums, generalized oedema and ascites, pleural effusion, and enlargement of the liver and spleen. The results of laboratory tests conformed with the diagnosis of cirrhosis. X-ray examination showed oesophageal varices, and the patient died after a massive gastro-intestinal haemorrhage. The necropsy findings were compatible with a diagnosis of post-necrotic cirrhosis; there were numerous varices of the oesophagus, and in one of these a large defect was present.

A review of the literature shows that a probable relationship to infective hepatitis appears likely in many of the reported cases, including cases marked by an acute illness with definite gastro-intestinal symptoms; in some of these cases, moreover, evidence suggestive of hepatitis was obtained from a biopsy specimen taken at an early stage of the disease. There remain, however, a number of cases which showed no previous history of infective hepatitis or acute illness which might have been non-icteric hepatitis or of exposure to known hepatotoxins. Some of these cases had the typical picture of cirrhosis, as in the case here described. In other cases the usual clinical and histological picture of cirrhosis was present, but an additional factor appeared to be involved; thus there were additional findings suggestive of an abnormal endocrine influence in one group and of lupus erythematosus in a further group. It is suggested that further investigation of the aetiology of these various manifestations is required. *Joseph Parness*

PANCREAS

965. Pancreatitis and Renal Insufficiency

H. V. FREIDELL. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 487–492, Nov., 1960. 16 refs.

Patients who have acute pancreatitis together with acute renal failure present difficult problems of diagnosis and treatment. This paper describes 3 cases in which the patient was gravely ill with signs of acute renal failure; the presence of pancreatitis was suspected in Case 1, there was a recent history of pancreatitis in Case 2, but in Case 3 pancreatitis was not known to be present. The serum amylase level in Cases 1 and 2 was 1,029 and 833 Somogyi units per 100 ml. respectively. Fluid obtained by peritoneal aspiration in Case 2 had an amylase content of 714 Somogyi units per 100 ml.; peritoneal aspiration in Case 1 was negative for fluid. The patients were receiving careful conservative therapy for acute tubular necrosis, but all deteriorated with profound shock; when deterioration appeared, vasopressor agents, antibiotics, blood transfusion, and steroid therapy were added or increased without apparent success. All 3 cases terminated with irreversible shock and death. The necropsy findings showed acute haemorrhagic pancreatitis together with acute tubular necrosis in all cases.

It is known that the serum amylase level may be raised in pancreatitis, in renal disease, and in various other conditions; therefore such a finding is not diagnostic. The amylase content of the peritoneal fluid was significant, however, in one of the cases described here. The problems of diagnosis and treatment are discussed, the recent literature concerning cases in which the two conditions were present is reviewed, and the experiences of various authors are collated. It is concluded that the fatal shock in the cases described was most probably caused by bacterial endotoxins. The following measures which may prove useful in treatment are noted: the early administration of propylthiouracil to arrest pancreatic necrosis; the prophylactic use of reserpine and dibenamine to counter the refractory state of small vessels; and the early institution of steroid therapy to prevent the initial shock of bacterial endotoxins.

Joseph Parness

966. Chronic Relapsing Pancreatitis. Fate of Fifty-six Patients First Encountered in the Years 1939 to 1943, Inclusive

E. E. GAMBILL, A. H. BAGGENSTOSS, and J. T. PRIESTLEY. *Gastroenterology* [*Gastroenterology*] **39**, 404–413, Oct., 1960. 1 fig., 2 refs.

The authors describe the fate of 50 patients (out of a total of 56) with chronic relapsing pancreatitis first seen at the Mayo Clinic during the period 1939 to 1943. The ratio of males to females was 4·2:1. A follow-up study carried out in 1959 revealed that of these patients, 33 had died, 10 directly from pancreatitis or its complications (diabetes in 5, pancreatitis in 4, and haemorrhage in one), while most of the other 23 died from unrelated vascular, respiratory, neoplastic, or abdominal conditions. In 54 of these cases the mean age at onset of attacks of pain was 37·6 (range 10 to 75) years, but 44·6 years at first admission to the clinic. In 25 patients the disease had lasted more than 10 years, and in 9 cases the duration ranged from 20 to 45 years. In regard to complications, of the original 56 patients, 30 (53·6%) developed diabetes at a mean interval of 9 years after the pain started, 24 (42·9%) had steatorrhoea at a mean of 8·2 years later, and 22 (39·3%) had pancreatic calcification at a mean period of 8·8 years afterwards. Gastro-intestinal haemorrhage occurred in 9 cases (16·1%), related abscesses in 7 (12·5%), ascites in 6 (10·7%), and various intra-abdominal venous thromboses in 5 (8·9%). Many of the patients were [not unexpectedly] chronic alcoholics.

Pathological data obtained at necropsy or by biopsy in 21 cases showed constant interstitial fibrosis, lymphocytic infiltrations, and residual areas of necrosis in the pancreas. Less commonly observed were dilatation of the ducts, suppuration, complete fibrous replacement, atrophy of the islets of Langerhans, and arteriosclerosis. The authors suggest that various operations may often have relieved the pain and benefited the patients [though this was hotly disputed in the subsequent discussion, in particular as most of the operations were on the biliary tract, which was involved in only 27 of the cases]. Of 48 traced surgical cases there had been complete and permanent relief in 18 (37·5%) within a few months of operation. The authors conclude that patients with chronic pancreatitis do better than was originally expected to be the case.

[This is an interesting and fundamental paper.]

Arnold Pines

Cardiovascular System

967. **Giant-cell Arteritis, or Arteritis of the Aged**
J. W. PAULLEY and J. P. HUGHES. *British Medical Journal* [*Brit. med. J.*] **2**, 1562–1567, Nov. 26, 1960. 27 refs.

Between 1953 and 1959 the authors saw and treated at Ipswich hospitals 76 cases of arteritis of the aged ("giant-cell arteritis", "temporal arteritis"), which, they consider, is a common condition and frequently overlooked. The ages of the patients at the onset of the illness ranged from 54 to 88 years. The following 14 forms of presentation of the disease are described: (1) classic "temporal arteritis"; (2) head pains and headache and tenderness without classic stigmata; (3) facial neuralgia; (4) madness (confusion, depression, dementia); (5) visual; (6) cardiac ischaemia; (7) "anarthritic" rheumatism; (8) pain in the ear, vertigo, deafness; (9) strokes; (10) vomiting and cachexia suggesting neoplastic disease; (11) masquerading as meningeal irritation or subarachnoid haemorrhage; (12) pyrexia of unknown origin; (13) polyarthritis; and (14) aortic-arch syndrome.

Biopsy specimens of the artery were obtained in 23 cases; 21 were positive, 10 of them containing giant cells. The authors consider from experience that biopsy is not now justifiable, at any rate in the very elderly. The condition can be diagnosed on clinical grounds with due attention to the natural history of the disease, the symptoms and signs, especially in the eye, and the finding of a high erythrocyte sedimentation rate and abnormal protein electrophoresis. Steroid therapy, usually with prednisolone in a dosage of 10 mg. 2 or 3 times a day, is markedly beneficial, but should be discontinued gradually after 6 to 12 months.

[The abstracter remains in doubt whether the authors of this provocative paper have sufficiently delineated "arteritis of the aged" from non-inflammatory degenerative diseases of the arteries. He also questions the validity of such statements as "a depressive state, often concealed, invariably precedes the somatic manifestations of the disease".] *Bernard Isaacs*

968. **Sarcoid Heart Disease.** [Review Article]
G. H. PORTER. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 1350–1357, Dec. 29, 1960. 3 figs., bibliography.

969. **Acute Non-specific Pericarditis**
W. G. A. SWAN. *British Heart Journal* [*Brit. Heart J.*] **22**, 651–659, Nov., 1960. 4 figs., 18 refs.

Despite frequent reports of acute non-specific pericarditis from the United States in the past two decades, physicians in the United Kingdom seem to have remained somewhat sceptical about the diagnosis. The present paper reports 14 cases from Newcastle upon Tyne General Hospital and includes the third recorded fatal example of the disease. Necropsies in these 3 cases provided no evidence of tuberculosis, rheumatism, or other specific aetiology.

Acute non-specific pericarditis is predominantly a disease of males and recurrences are not uncommon. Pain and pericardial friction are occasionally absent. It is readily mistaken for a myocardial infarction, and of course anticoagulants may be dangerous. The illness is usually benign, but it can run a long course with frequent relapses, tamponade and later constriction having been reported. [It is difficult to exclude for certain a tuberculous aetiology in such cases, even histologically after operation.] Treatment is mainly expectant, but there is some reason for believing that steroid therapy may be helpful in severe cases.

The author postulates more than one cause for the condition. That it can be a virus infection seems to have been established (though virus studies in 3 of his cases were unfruitful), but its occurrence after operations and wounds of the heart and after cardiac infarction suggests that an autoimmune reaction may be responsible in some circumstances. *T. Semple*

970. **Right-sided Bacterial Endocarditis**
F. A. BASHOUR and C. P. WINCHELL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 411–416, Oct., 1960. 1 fig., 20 refs.

In this paper from the University of Texas Southwestern Medical School, Dallas, and the University of Minnesota Hospitals, Minneapolis, the authors report 10 cases of bacterial endocarditis affecting the right side of the heart which they have seen since 1951. The patients were all adults and 7 of them had congenital cardiac lesions (ventricular septal defect in 4 and patent ductus arteriosus, anomalous pulmonary venous drainage, and pulmonary stenosis with corrected transposition of the great vessels in one each). In 2 of these patients, in whom an atrial septal defect was also present, this defect was free from vegetations. In the 3 patients who developed the disease in the absence of congenital heart lesions the affected tricuspid valves were apparently normal, though idiopathic pulmonary hypertension was present in one and there was evidence of healed rheumatic disease of the mitral valve in another. Positive blood cultures were obtained from 8 patients, one of whom had 2 attacks. The organisms recovered were *Streptococcus viridans* (4), enterococcus (2), *Staphylococcus aureus* (2), and *Aerobacter aerogenes* (1). In the 2 patients with negative blood cultures the illness ran an acute course and it was thought that these might also have been staphylococcal infections.

Only 3 patients recovered, all of whom had infections due to *Strep. viridans*. The fourth patient with *Strep. viridans* endocarditis recovered from this attack, but died later from an enterococcal infection. Pulmonary in-

volvement from multiple septic emboli was thought to be the main factor responsible for death in all the fatal cases. One patient died suddenly after a profuse pulmonary haemorrhage. The authors conclude that important factors in the causation of right-sided bacterial endocarditis are the virulence of the infecting organism and intracardiac trauma to the right side of the heart, especially in the form of increased pressure.

Michael Harington

DIAGNOSTIC METHODS

971. **The Dependence of Vectorcardiographic Changes on the Pressure in the Pulmonary Circulation in Patients with Mitral Valvular Disease.** (Зависимость изменений векторкардиограммы от величины давления в малом круге кровообращения у больных с митральными пороками сердца)

V. I. Makolkin, I. I. Sivkov, and N. L. Jastrebcova. *Терапевтический Архив* [*Ter. Arh.*] **32**, 14–22, Oct., 1960. 5 figs., 14 refs.

In this study Akulinichev's precordial technique was used in the investigation of 67 patients, 39 women and 28 men, with mitral valvular disease. Pressures in the pulmonary artery and right ventricle were measured directly and the degree of hypertrophy was assessed by means of vectorcardiograms. Of 27 patients with a pulmonary arterial pressure over 100 mm. Hg the vectorcardiogram indicated the presence of right ventricular hypertrophy in 19, of hypertrophy of both ventricles in 7, and of partial right bundle-branch block in one. In no case in this group was the vectorcardiogram normal, nor was there any evidence of left ventricular hypertrophy. In a second group of 28 patients, in whom the pressure in the right ventricle was between 50 and 100 mm. Hg, right ventricular hypertrophy was found in 7, hypertrophy of both ventricles in 6, left ventricular hypertrophy in 5, and partial right bundle block in 3, while the tracing was normal in 7; this last finding, however, does not exclude a minor degree of hypertrophy. Of 12 patients with right ventricular pressures between 30 and 50 mm. Hg, right ventricular hypertrophy was seen in only one, combined hypertrophy in 2, and left ventricular hypertrophy in 5, while the vectorcardiographic tracings were normal in 4. Vectorcardiographic changes depend on the associated lesions in other valves.

The changes in the vectorcardiogram after the performance of commissurotomy were studied in 33 patients. They consisted in a reduction in the QRS loop area and anticlockwise rotation of the loop round its sagittal axis, with resulting deviation of the main axis to the right, up to and even past the vertical. In many cases the vectorcardiogram had returned to normal or almost normal. These changes were observed 1 to 5 months after the operation and were accompanied by clinical improvement. It is stated that, generally speaking, the vectorcardiographic changes following operation were more striking in those patients in whom the preoperative vectorcardiogram showed right or combined ventricular hypertrophy than in those in whom the preoperative tracing was normal or indicative of left ventricular hypertrophy. In all cases the changes resulted from alteration in the haemodynamics of the pulmonary circulation.

S. W. Waydenfeld

972. **Gastro-intestinal Lesions Affecting the Electrocardiogram: a Report of Three Cases**

J. B. McGuinness. *Scottish Medical Journal* [*Scot. med. J.*] **5**, 485–489, Nov., 1960. 5 figs., 15 refs.

Details are given of 3 patients—admitted to one medical ward of the Western Infirmary, Glasgow, within the same year—in whom alimentary-tract lesions simulated coronary arterial disease, electrocardiographically as well as clinically. All 3 patients were males, aged 67, 58, and 63 respectively. In Case 1, in which the cause of the trouble was an impacted sweet in the oesophagus, the electrocardiogram showed ST depression in the standard leads and in Leads aVf and V6, with a tall R in V2. The blood pressure was 100/70 mm. Hg, rising subsequently to 140/90 mm., and the erythrocyte sedimentation rate (E.S.R.) 15 mm. in the first hour. In Case 2, in which the final diagnosis was cholecystitis, the electrocardiogram showed potential (Grade-1) heart block and the blood pressure was 100/70 mm. Hg, rising subsequently to 120/70 mm. In Case 3, in which the final diagnosis was hiatus hernia, the electrocardiogram showed T_3 inversion, the blood pressure was 175/100 mm. Hg, and the E.S.R. 5 mm. in the first hour. In all 3 cases the electrocardiogram subsequently returned to normal. In the case of hiatus hernia the original electrocardiographic findings were reproducible by placing the patient in the left lateral position and, to a lesser extent, in the standing position.

[An interesting trio of cases emphasizing the need for caution in diagnosing coronary arterial disease in this coronary-conscious era.) *William A. R. Thomson*

973. **The Relationship of the Electrocardiographic Pattern of Potassium Depletion to the Concentration of Potassium in Red Blood Cells**

L. A. Soloff, S. A. Kanosky, and J. H. Boutwell Jr. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 280–290, Sept., 1960. 3 figs., 16 refs.

The frequent lack of correlation between a characteristic pattern of potassium depletion in the electrocardiogram (ECG) and the serum potassium level led the authors, working at Temple University School of Medicine and Hospital, Philadelphia, to investigate the relation between the ECG and the potassium concentration in the erythrocytes. The range of potassium concentration in the erythrocytes of 16 normal subjects was 90 to 104 mEq. per litre. To 17 subjects, 13 with and 4 without cardiac disease, with normal potassium concentrations in the serum and erythrocytes 1 g. of chlorothiazide was given daily for 8 days. In 5 with cardiac disease the serum potassium concentration had by then fallen below normal and the regimen was continued until signs of hypopotassaemia appeared in the ECG or until the patient asked that it be stopped. Investigations in this group showed marked discrepancies between the serum and erythrocyte potassium concentrations and the ECG findings. In another 52 patients, in whom the

clinical condition or ECG suggested the possibility of hypopotassaemia, the potassium concentrations in the serum and erythrocytes were also investigated. ECG findings suggestive of hypopotassaemia were present in 9 out of 13 cases in which the serum potassium concentration was normal and that in the erythrocytes low, in 5 out of 8 cases in which both concentrations were low, and in none of 5 cases in which a low serum potassium concentration was accompanied by a normal concentration in the erythrocytes.

The authors conclude that signs of potassium depletion in the ECG are associated with a low concentration of potassium in the erythrocytes, irrespective of the serum potassium concentration, though there is no quantitative relation between the degree of potassium deficiency in the erythrocytes and the degree of change in the ECG. In certain complex arrhythmias estimation of the potassium concentration in the erythrocytes may help in the differentiation between those due to digitalis intoxication with potassium depletion and those caused by intrinsic myocardial disease. *A. Schott*

974. **Electrocardiographic Changes following the Administration of Thyroid Stimulating Hormone (Thyrotropin)**

S. P. BAKER, M. LANDOWNE, and G. W. GAFFNEY. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 905–914, Nov., 1960. 4 figs., 9 refs.

The electrocardiographic (ECG) changes following administration of thyroid stimulating hormone (T.S.H.) to 5 euthyroid normotensive men aged 46 to 92 years are described in this paper from the National Heart Institute, Bethesda, and the Baltimore City Hospitals. The T.S.H. was administered intramuscularly in a daily dose of 25 mg. (10 *U.S.P.* units) for 4 to 5 days. In 2 patients there were no significant ECG changes, but the remaining 3 showed premature beats, " coving " and depression of the S–T segment, and T-wave inversion; no consistent alteration of the QRS complex occurred. These changes preceded such signs as increase in the heart rate, basal metabolic rate, uptake of ^{131}I, and serum protein-bound iodine level which are indicative of hyperthyroidism, and they regressed soon after T.S.H. was withdrawn.

Among the possible causes of these ECG changes the authors mention a direct effect of T.S.H. on the myocardium, cardiac effects of thyroid hormone preceding the general systemic effects, and potentiation of the effects of adrenaline and noradrenaline. They conclude that T.S.H. can produce electrocardiographic changes characteristic of increased myocardial irritability and altered repolarization, and suggest that sympathomimetic factors may be involved. *Gerald Sandler*

975. **The Electrocardiogram in Thyrotoxicosis**

I. HOFFMAN and R. D. LOWREY. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 893–904, Nov., 1960. 6 figs., 33 refs.

The electrocardiograms (ECGs) of 123 patients with thyrotoxicosis have been studied at the County General Hospital (University of Southern California), Los Angeles. Patients with evidence of associated hypertensive, ischaemic, syphilitic, or rheumatic heart disease and also those receiving digitalis therapy were excluded from the study, in which standard 12-lead electrocardiography was employed. In 28 patients (22·7%) the ECG showed ST–T changes, frequently transient in most leads, consisting of elevation and " coving " of the S–T segment associated with T-wave inversion; 13 of these patients were females aged from 20 to 30 years. The Q–T interval (corrected for heart rate) was shortened in 18 patients (17%), 13 of whom showed the ST–T changes also. A prolonged P–R interval occurred in 11 patients (8·9%), 6 of them also having ST–T changes. Atrial fibrillation occurred in 15 patients. Six illustrative cases are described.

The possible causes of these abnormalities in the ECG are considered, the factors discussed including the role of adrenaline, myocardial infiltration under the influence of thyrotrophin, and autonomic imbalance. The authors conclude that thyrotoxicosis can produce distinctive changes in the ECG, the cause of which, they suggest, is neurohumoral factors.

[No reference is made to the incidence of cardiac enlargement, atrial fibrillation, or congestive failure in relation to the electrocardiographic abnormalities. Since all of these cardiac complications of thyrotoxicosis may, by themselves, influence the ECG considerably the present study is inadequate and the conclusions unjustified.] *Gerald Sandler*

976. **The Vectorcardiogram in the Differential Diagnosis of Atrial Septal Defect in Children**

J. LIEBMAN, and A. S. NADAS. *Circulation* [*Circulation*] **22**, 956–975, Nov., 1960. 16 figs., 24 refs.

At the Children's Medical Center (Harvard Medical School), Boston, vectorcardiography was carried out on 135 normal children aged 2 to 14 years, 32 patients with atrial septal defects (A.S.D.) of the ostium secundum type and 23 with A.S.D. of the " endocardial cushion " type (embracing ostium primum lesions with or without ventricular septal defect (V.S.D.) or atrioventricular valve clefts), together with 6 patients who did not fit clearly into either group but had evidence of left-to-right shunts at atrial level. (At operation 2 of these 6 were found to have V.S.D. with tricuspid regurgitation and the other 4 to have ostium secundum defects with mitral or tricuspid valve clefts.)

The vector loops of normal patients were predominantly to the left, whereas those of both main groups of patients with A.S.D. were approximately as far to the right as to the left, indicating right ventricular hypertrophy. While the anterior and posterior forces were of equal magnitude in the normal tracings, the anterior force predominated in those of both A.S.D. groups. The inferior forces predominated in the normal subjects and in those with ostium secundum lesions, but the superior forces were the greater in those with endocardial cushion defects. The linear measurements in the 4 cases of A.S.D. of ostium secundum type with clefts of the atrioventricular valves were similar to those in cases of ostium secundum lesions in general and, in contrast to the clinical picture, differed sharply from those of the group with endocardial cushion defects. No conclusions

could be drawn from the tracings in the 2 cases of V.S.D. with tricuspid valvular defects. The mean electrical axis as determined from the frontal QRS vector loop ranged from +20° to +80° in the normal subjects. In the group with ostium secundum defects the mean axis was considerably to the right of normal and in the group with endocardial cushion defects it was far to the left. Of the 4 atypical cases of A.S.D. of ostium secundum type, in 3 the mean electrical axis was over +90°. In one case of proven A.S.D. of ostium secundum type no axis could be determined in the frontal plane of the electrocardiogram, whereas in the vectorcardiogram the axis was +120°.

The majority of patients in the two major groups had similar patterns in the horizontal plane. In the frontal plane, however, the QRS loops in the ostium secundum group were inferior and most of them were inscribed in a clockwise direction, whereas in the endocardial cushion group the loops were superior and mostly counterclockwise. Clockwise inscription in both groups seemed to indicate a high right ventricular work load. A correlation was attempted between vectorcardiographic and haemodynamic data in 22 cases from each of the main groups. The ratio of right ventricular:left ventricular work appeared to be closely related to the vectorcardiographic appearances—as the work ratio increased the anterior and rightward forces also gradually increased.

The authors state that practically all patients with A.S.D. have right ventricular hypertrophy, but that by any definition right bundle-branch block is not constantly found. Whereas the vectorcardiogram may reveal no more than does vectorial analysis of the electrocardiogram (ECG) in differentiating ostium secundum defects from endocardial cushion defects, it is helpful in differentiating unusual cases, such as the 6 included here, from both groups. The superior position of the vector loop (left axis deviation in the ECG) characteristic of an endocardial cushion defect is thought to be secondary not to left ventricular hypertrophy, but to a congenital anomaly in the conducting system. *R. S. Stevens*

CONGENITAL HEART DISEASE

977. **Patent Ductus Arteriosus in Infancy**
O. Scott and G. F. Gearty. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] 35, 465–474, Oct., 1960. 6 figs., 16 refs.

Patent ductus arteriosus in infancy may be a serious condition, lacking the features which make it easily detected in older children, yet it can be surgically corrected with little risk. In 28 cases seen at the Royal Liverpool Children's Hospital the common presenting signs were dyspnoea, especially on feeding, and bronchitis, which was often recurrent. Four infants had congestive heart failure with oedema and liver enlargement. The pulse was "water-hammer" in all, this characteristic being felt more easily at the ankle than at the wrist. The heart murmur did not have the classic "machinery" quality, but in 22 cases the systolic murmur was, at the pulmonary area, continued past the second sound, and a thrill was felt in 12. The remaining 6 had a murmur confined to systole. In 18 there was also an apical mid-diastolic murmur.

Radiography revealed some degree of pulmonary plethora in all and a suggestion of left ventricular enlargement in 18 cases. Cardiograms showed hypertrophy of both ventricles in 4, of the left ventricle alone in 11, and of the right alone in one.

Cardiac catheterization, performed in 4 cases in which the diagnosis was uncertain, showed pulmonary hypertension, which was of systemic degree in 3; one infant had a normal pulmonary pressure at recatheterization a year after surgical closure of a ductus 14 mm. in diameter. In 24 of the 28 infants the ductus was closed surgically with good result; the other 4 died of multiple abnormalities or infections.

Attention is drawn to the similar physical findings in cases of truncus arteriosus, in which there is usually cyanosis too, and to the danger of closing a ductus which is serving a compensatory purpose, as in tricuspid valvular atresia. *J. A. Cosh*

978. **Persistence of the Ductus Arteriosus in Infancy. A Clinical and Haemodynamic Study with Results of Operation.** (La persistance du canal artériel chez le nourrisson. Étude clinique et hémodynamique; résultats opératoires)
J. Nouaille, M. Thibert, P. Lucet, M. Gautier, J. Mathey, J. P. Binet, and J. J. Galey. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur.*] 53, 961–985, Sept. [received Nov.], 1960. 9 figs., 24 refs.

Of 56 children with patent ductus arteriosus (excluding 5 who died soon after admission) seen at the Hôpitaux de Bicêtre and Laënnec, Paris, the condition was simple and uncomplicated by pulmonary hypertension in 14. The latter patients were symptom-free and well-grown, developed the typical continuous murmur in most cases by the age of 2 years, and were all treated successfully by operation.

In the remaining 42, in whom there was also pulmonary hypertension, symptoms of breathlessness and respiratory infection were common, and most of them were under-weight. Only 10 had a continuous murmur, and the remainder had a systolic murmur to the left of the sternum, sometimes with a thrill, or a diastolic murmur; the peripheral pulses were vigorous in all. Radiography revealed cardiac enlargement in all but a few cases, accompanied by prominent pulmonary arteries and pulmonary plethora, while cardiography showed hypertrophy of the left ventricle or of both ventricles. In 32 of the 33 investigated by cardiac catheterization proof of the persistence of the ductus was obtained by passage of the catheter through it. Generally, the shunt of oxygenated blood into the pulmonary artery was equivalent to 2 volumes of oxygen per cent.; it was less (as was also the pressure gradient between the aorta and the pulmonary artery) in cases with severe pulmonary hypertension. In two-thirds of these patients the pulmonary arterial systolic pressure was 50 mm. Hg or greater, mostly accompanying a large shunt. The authors note that in such cases the surgical closure of the

ductus must be regarded as a matter of some urgency. When the pulmonary arterial pressure is high and the shunt small the presence of an additional defect must be suspected.

In regard to treatment, cardiac failure and respiratory infection call for treatment with digitalis, mercurial diuretics, and antibiotics, followed by operation as soon as possible. The presence of an isolated patent ductus is confirmed if, at operation, clamping of the ductus causes an immediate fall in pulmonary arterial pressure. Surgical closure may occasionally result in a postoperative period of systemic hypertension and even left ventricular failure. Subsequent physical improvement is striking and there is a rapid gain in weight. Of the 51 patients treated surgically, 6 died (5 having pulmonary hypertension and an additional defect), but the remainder improved dramatically. *J. A. Cosh*

979. **Congenital Bicuspid Aortic Valve.** (La bicuspidie aortique congénitale)
P. Soulié, J. Di Matteo, M. Caramanian, D. Colonna, and J. Audoin. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur.*] 53, 1203–1222, Nov., 1960 [received Jan., 1961]. 11 figs., 4 refs.

The authors describe 18 cases of congenital bicuspid aortic valve seen among 396 patients with heart disease examined post mortem between 1954 and 1959—an incidence of 4·5%; of the 18 patients, 12 were male and 6 female. Aortic valvular disease was diagnosed clinically in 9 cases; in 8 of these it was an isolated lesion, taking the form of aortic stenosis in 3 cases, of aortic insufficiency in 4 (one with bacterial endocarditis), and of both stenosis and insufficiency in one. In the 9th case aortic stenosis was associated with coarctation of the aorta. In the other 9 cases the anatomical abnormality had given rise to no clinical signs; in 7 cases it was discovered at necropsy in association with congenital heart malformation. In the remaining 2 cases it was an incidental finding, in one subject who died of myocardial infarction and in one dying of cardiac failure of ischaemic origin. The age at death varied from 7 months to 65 years.

The authors then describe the various anatomical types of the condition, which they designate (1) sagittal (found in 7 of their cases), (2) frontal (8 cases), and (3) oblique (3 cases), and discuss the distinction between congenital and acquired anomalies of this kind. Of the 18 cases, the valves appeared to be healthy in only 3, in 5 others only slight changes were present, but in the remaining 10 obvious secondary changes were found. These changes, which are described in detail, consisted in stenosis, incompetence, calcification, eversion, or other abnormalities. In 2 cases bacterial endocarditis had affected the valves. Anatomically the malformation was the sole lesion in only 4 cases, associated congenital cardiac lesions being present in the other 14. In 11 of these the malformation was obvious, taking the form of calcified stenosis of the aorta in 7 cases, alone in 2 of them and associated with aortic dilatation, dilatation of the posterior sinus of Valsalva, patent foramen ovale, persistent ductus arteriosus, and congenital mitral stenosis in one case each. In the remaining 4 there was respectively aneurysm of the sinus of Valsalva, bicuspid pulmonary valvular disease, patent interventricular septum, and a complex malformation consisting of the tetralogy of Fallot and an aorto-pulmonary fistula. Lastly, in one case a minor malformation of the pulmonary valve was present, while in 4 an unusual conical-cylindrical dilatation of the proximal part of the aorta extended from the aortic ring to the region of the isthmus.

In conclusion the authors discuss at some length the literature on congenital bicuspid aortic valves and point out that the congenital alterations in the aortic wall described above predispose to rupture and dilatation or ectasia of the sinuses of Valsalva and explain certain dilatations of the ascending aorta associated with the valvular lesion.

[For full details this paper should be read in the original.] *R. Wyburn-Mason*

MYOCARDIUM

980. **Bilateral Ventricular Hypertrophy Due to Chronic Pulmonary Disease**
N. Michelson. *Diseases of the Chest* [*Dis. Chest*] 38, 435–446, Oct., 1960. 1 fig., 21 refs.

The necropsy findings in 32 cases of bilateral ventricular hypertrophy in adult males are analysed. In none of the cases were there congenital cardiac abnormalities, coronary disease, or hypertension, and all showed severe chronic pulmonary disease. Electrocardiographic tracings in the absence of digitalis therapy were available for study in 27 of the cases. The thickness of the ventricular walls (right and left) was measured and the relative increase between the two sides noted. Hypertrophy of the right ventricle was found to be relatively greater than that of the left, right ventricular hypertrophy being reflected by the appearance of right axis deviation in the electrocardiogram. Other interesting but less important electrocardiographic findings are also described. It is suggested that bilateral ventricular hypertrophy in chronic pulmonary disease is more common than has been realized. *J. B. Wilson*

981. **Spontaneous Rupture of the Heart**
A. Levene. *British Heart Journal* [*Brit. Heart J.*] 22, 660–670, Nov., 1960. 11 figs., 28 refs.

This is a statistical and pathological study from the Royal Marsden Hospital, London, of 16 hospital cases of cardiac rupture (from the records of University College Hospital, London, 1931–56) and 563 examples from the records of the coroner for the Northern district of London (from which the necropsy findings in 50 cases are discussed). The hospital figure represents an incidence of 12·5% of fresh cardiac infarcts; the coroner's figures showed great annual fluctuation, but increased prevalence in the winter months was consistent.

In the fresh, unfixed specimen of the ruptured heart one can readily see the haemopericardium, the thrombus adherent to the endocardial surface, the lacerated area underlying the thrombus, which is considerably longer

than the epicardial tear, and the softness of the necrotic muscle, through which a finger can be pushed with ease. Infarcts that rupture occur in the same sites as, and with similar relative frequency to, those that do not. Hearts showing less arteriosclerosis and fewer developed collaterals are more prone to rupture when infarction occurs. The condition is more common in old age, probably because of hypertension and relative absence of left ventricular hypertrophy. It is believed that rupture is usually a very early complication of transmural infarction, even before the fifth day. Gross myocardial scarring is never, and cardiac aneurysm rarely, associated with rupture.

With a small lateral infarct all that one can observe is a zigzag line through a small area of myocardium. With infarcts above 2 cm. in diameter rupture usually occurs through or near one edge of the infarcted area and, as a result of oblique tracking, the epicardial tear may be some 2 cm. away from the internal opening. With antero-septal infarcts rupture usually takes place at the junction of the left ventricular wall with the septum, either into the right ventricle or through the left ventricular wall. Tears of the interventricular septum originate on the left ventricular aspect of the septum, and the opening there is much larger than that on the right ventricular surface. These septal perforations are rare although septal infarct is common, probably because full-thickness infarcts of the septum are unusual.

T. Semple

982. **Friedreich's Ataxia: a Neurocardiac Disease**
J. M. HARTMAN and R. W. BOOTH. *American Heart Journal* (*Amer. Heart J.*] **60**, 716–720, Nov., 1960. 10 refs.

The authors report that of 7 cases of Friedreich's ataxia seen at Ohio State University Health Center, Columbus, since 1954 the electrocardiogram was abnormal in the 6 cases in which it was recorded. Clinical evidence of heart disease was found in only one patient, a woman aged 33 who when first seen had frequent ventricular extrasystoles, a low-voltage QRS, and minimal non-specific changes in the T wave. Three years later she developed auricular fibrillation, which was converted to atrial flutter by performance of a 2:1 atrio-ventricular block with lanatoside C, but later reverted to auricular fibrillation. A year later when again seen she had a supraventricular tachycardia fluctuating between atrial flutter and fibrillation; this was converted to sinus rhythm with quinidine, but relapsed 18 months later. Of the other 5 cases examined electrocardiographically, one showed auricular fibrillation, 2 incomplete right bundle-branch block, and 2 symmetrical T-wave inversion, low voltage and non-specific T-wave changes being the most common findings. No organic murmurs were heard in any of the patients. On the basis of these findings and the fact that in every case of Friedreich's ataxia examined post mortem hitherto reported in the American and British literature abnormal findings in the heart, usually chronic interstitial myocarditis, were described, the authors conclude that Friedreich's ataxia is a neurocardiac disease, involving the heart as well as the central nervous system. *I. Ansell*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

983. **Testosterone Combined with Vitamin B_{12} in the Treatment of Coronary Atherosclerosis.** (Лечение коронарного атеросклероза тестостероном в сочетании с витамином B_{12})
L. G. FOMINA. *Терапевтический Архив* [*Ter. Arh.*] **32**, 58–61, Oct., 1960. 2 refs.

In addition to causing vasodilatation the sex hormones induce a rise in the myocardial content of glycogen, nitrogen, and phosphates, improve the nutrition of the myocardium, and reduce the creatinuria which results from incomplete utilization of creatine by the ageing muscle.

In the present study the effect of the sex hormones was enhanced by the addition of vitamin B_{12} because of the known choline-sparing activity of the latter. Treatment, consisting of 15 to 25 mg. of testosterone propionate intramuscularly daily and vitamin B_{12} in a dose of 30 to 50 μg. on alternative days for a period of 24 to 30 days, was given to 18 male in-patients and 25 male out-patients aged between 40 and 69 years; during treatment most of the 25 out-patients remained at work. Of the total number of patients, 7 had had one, and 2 had had repeated episodes of myocardial infarction. The diet of 34 had contained much meat and fat, 27 smoked excessively, and 40 had been under considerable nervous tension at work. Also 20 patients showed a tendency to obesity and 10 were definitely obese, while there was a long history of hypertensive disease in 22 patients, of angina of effort in 26, and of angina both on effort and at rest in 17. As a result of the course of treatment 26 of the 43 patients improved considerably. The attacks of angina ceased, exercise tolerance improved, and fat metabolism showed a change for the better. A further 6 patients lost the typical attacks of anginal pain but continued to experience periodically nagging or sharp pain in the praecordium. The remaining 11 patients showed only slight improvement, although the attacks were reduced in intensity and frequency and there was improved exercise tolerance and some general improvement. These poor results occurred in patients with marked structural changes in the coronary vessels and in those who remained ambulatory. The serum cholesterol level was reduced in 29 patients from between 146 and 464 mg. to between 12 and 176 mg. per 100 ml. In 9 patients there was no change in the cholesterol level and in 5 an average rise of 36 mg. per 100 ml. was observed. The lecithin:cholesterol ratio, which was below 1·0 in 18 patients, increased in 21, diminished in 7, and remained unchanged in 15. *S. W. Waydenfeld*

984. **Prognosis and Anticoagulant Prophylaxis after Coronary Occlusion**
J. MCMICHAEL and E. H. O. PARRY. *Lancet* [*Lancet*] **2**, 991–998, Nov. 5, 1960. 8 figs., bibliography.

The first part of this paper from the Postgraduate Medical School of London is a review of a number of the larger follow-up studies of patients who have had

coronary occlusion, covering over 5,000 patients in all. Comparison of year-by-year survival rates shows a number of differences between the component series, due to case selection, with an average survival rate at 5 years of 65% to 70%. Prognosis is better in younger patients, in those making a complete clinical recovery, and in those of better social status (the 5-year survival rate in a group of doctors being 82%). Prognosis is noticeably worse if congestive failure results from the infarct, if shock and pain are prolonged, in diabetics, and in hypertensives who have cardiac enlargement and advanced retinopathy.

The second part assesses reports of the results of long-term anticoagulant therapy. While this treatment undoubtedly improves the outlook in the acute illness, particularly by reducing thrombosis and embolism, the authors find the claims for the benefits of long-term treatment unproven. Most reported series are too small to be reliable and use control groups whose prognosis is worse than usual, while the prognosis of the treated cases lies within the normal untreated range.

In two large and well controlled series (Bjerkelund, *Acta med. scand.*, 1957, **158**, Suppl. 330, and Medical Research Council, *Brit. med. J.*, 1959, **1**, 803; *Abstr. Wld Med.*, 1959, **26**, 93) the protective effect of anticoagulants was largely confined to the early months of treatment and to patients under 55 or 60 years of age. This, it is suggested, may derive from some effect of treatment upon the healing process of the infarct. The differing pathogenesis of arterial and of venous thrombosis, too, makes it likely that anticoagulants will influence the latter but not the former. The dangers of anticoagulants include haemorrhage during treatment and thrombosis after its abrupt cessation. *J. A. Cosh*

985. **The Role of Effort and Occupation (Including Physicians) in Coronary Occlusion**
A. M. MASTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 942–948, Oct. 22, 1960. 16 refs.

The author here reports the results of an investigation in which a special questionary was completed from the clinical history in 2,600 cases of acute coronary occlusion seen by himself or his colleagues over a period of more than 25 years. Care was taken to exclude from the study cases of acute coronary insufficiency without occlusion, the diagnostic features of which are fully set out. Most of the patients came from New York City and its environs, and they included all types and social groups, from the physically very active to the most sedentary, and from those in the lowest to those in the highest income groups. In the questionary 17 distinct questions were listed, and although complete replies could not be obtained from the history in all cases, a significant total of answers was obtained in each category.

The conclusions arrived at [which indicate the points which were selected for detailed analysis] were as follows. Occupation, social status, effort, and rest play no part in causing this form of "heart attack". The truth of the dictum that coronary thrombosis is a "doctor's disease" is doubtful. One bout of acute coronary occlusion predisposes to another, but only on account of the underlying atherosclerosis. A patient who has recovered from coronary occlusion should return to work provided that it is not too arduous or mentally exhausting. Effort does not produce capillary haemorrhage in an intimal plaque of a diseased coronary artery. The only known cause of coronary occlusion is the presence of atherosclerosis, even in young patients. The only contributory cause of coronary thrombosis is physiological shock. Coronary disease is on the increase only on account of the ageing of the population, improved diagnosis, and recent changes in the classification of heart disease, and not because of the increased "stress and strain" of modern life.

The author believes that until the aetiology of atherosclerosis is better known it will not be possible to prevent or forestall attacks of coronary occlusion. He also expresses doubts of the value of long-term anticoagulant therapy in decreasing the incidence of coronary occlusion.

[This study, although open to certain criticisms, tends to upset many of the commonly held beliefs in regard to acute coronary occlusion.] *P. T. O'Farrell*

986. **Myocardial Infarction as a Complication of Major Gastro-intestinal Haemorrhage.** (Les infarctus du myocarde compliquant les grandes hémorragies digestives)
C. LABRAM, C. MACREZ, and M. MOUQUIN. *Presse médicale* [*Presse méd.*] **68**, 1925–1926, Nov. 19, 1960. 12 refs.

Severe anaemia, sudden collapse, and increased coagulability of the blood have all been impugned as precipitating factors in the causation of myocardial infarction in patients with advanced atheroma of the coronary arteries. Writing from the Hôpital Broussais, Paris, the authors point out that although these three factors all occur in massive haemorrhage, notably in that from the gastro-intestinal tract, it is nevertheless rare for massive haemorrhage to be responsible for causing infarction. When it does it is nearly always from the intestinal tract. Two such cases are reported. The first was that of a man aged 82 who was admitted to hospital 24 hours after copious haematemesis and melaena; for 6 months previously he had suffered from progressive anorexia and loss of weight. During the administration of a blood transfusion he developed agonizing presternal pain. There had been no error in the grouping of the transfused blood; an electrocardiogram gave clear evidence of infarction. He died 3 days later, and at necropsy a recent anterior infarct due to atheromatous stenosis of the left coronary artery was found. There was no thrombosis. The cause of the haemorrhage remained undetermined since the intestinal tract could not be examined, but severe anaemia, with an erythrocyte count of only 2,000,000 per c.mm. was deemed to have been the cause of the infarction. The second case occurred in a man aged 55 with a 7-year history of anginal attacks and who, 2 months before admission, had had a prolonged attack of presternal pain. In view of electrocardiographic evidence of infarction he was given anticoagulant therapy. Melaena necessitated his admission to hospital. The erythrocyte count did not rise above 2,000,000 per c.mm. in spite of repeated

blood transfusions. A further electrocardiogram revealed a posterior myocardial infarct. He died 6 days after admission and at necropsy an old anterior infarct and a recent posterior infarct were discovered, but no thrombosis. The coronary arteries were atheromatous, the right being stenosed for a distance of 2 cm. Haemorrhage was located in the colon in an area 25 cm. in length and was considered to have been caused by the anticoagulant therapy.

In discussion the authors urge that when confronted with gross intestinal haemorrhage in a patient old enough to have atheromatous coronary arteries or with antecedent anginal attacks the possibility of myocardial infarction should be borne in mind. The greater the degree of vascular collapse complicating the haemorrhage, the more certainly will the electrocardiogram reveal signs of ischaemia or necrosis. Meticulous treatment of both the shock and the anaemia remains the only hope of preventing a fatal issue in such cases. Moreover, in collapsed patients with myocardial infarction, with or without a known history of a previous gastro-intestinal lesion such as peptic ulcer, the possibility of unmanifested gastro-intestinal haemorrhage must be considered, since in such cases anticoagulant therapy may be disastrous. Infarction secondary to haemorrhagic digestive disorder is usually preceded by the onset or recurrence of anginal attacks, but it may be revealed by the electrocardiogram alone. The authors conclude that shock associated with vascular collapse is the commonest cause of infarction in patients with atheromatous coronary arteries. Anaemia is important as an aggravating cause of circulatory failure, but when it is severe as a result of massive haemorrhage it may *per se* increase the tendency to infarction. The aetiological significance of increased coagulability of the blood can only be surmised, although it has been shown experimentally that when severe haemorrhage is induced in dogs the later samples of blood coagulate more rapidly than do the early samples. Hypercoagulability is probably associated with haemoconcentration secondary to the haemorrhage.

E. S. Wyder

987. **Myocardial Infarction in Patients under Forty. Some Clinical, Aetiological, and Pathogenetic Problems.** (Инфаркт миокарда в молодом возрасте. Некоторые вопросы этиологии, патогенеза и клинического течения)

M. A. Gurevič. *Терапевтический Архив* [*Ter. Arh.*] 32, 46–55, Oct., 1960. 5 figs., 17 refs.

The author reports that in a series of 685 patients with myocardial infarction 46, 37 men and 9 women, (6·7%) were under the age of 40. Of these patients, 10 suffered from hypertensive disease, 8 had endarteritis obliterans, 8 various endocrine disorders (obesity, diabetes, or polyglandular insufficiency), 21 had a history of head injury followed by irritability, 30 were heavy smokers, and 17 were alcoholics. In 2 cases the infarction could have been a result of the development of rheumatic coronary arteritis and in 2 of thrombosis complicating erythraemia, while one patient showed evidence of syphilitic mesoaortitis. However, the main underlying cause in all cases was coronary atherosclerosis. In 30 cases the patient was employed on manual work, which in 19 required great physical effort. The special clinical features were conditioned by the absence of a collateral circulation and the high reactivity of the central nervous system. Warning signs before the infarction were absent in 29 of the 46 patients; in most cases the pain was very severe and vegetative disturbances such as vasomotor lability, disturbances of temperature regulation, polyuria, and marked leucocytosis were common.

The electrocardiographic changes were definite and persistent. The infarct was situated anteriorly in 6 cases, posteriorly in 11, anteriorly and encroaching on the interventricular septum in 12, antero-laterally in 11, postero-laterally in 3, and antero-postero-laterally in 2. A second episode of infarction occurred in 7 patients, while 8 developed cardiac aneurysm. Severe disturbances of cardiac rhythm or of conductivity and progressive circulatory failure were less common than in older patients, probably because of the better initial condition of the myocardium in these younger patients. Embolic phenomena were observed in 3 patients. Hypercholesterolaemia (blood cholesterol level over 200 mg. per 100 ml.) was found in only 5 cases. Four of the patients died.

S. W. Waydenfeld

988. **Lactic Dehydrogenase Activity in Acute Myocardial Infarction**

J. King and A. P. B. Waind. *British Medical Journal* [*Brit. med. J.*] **2**, 1361–1363, Nov. 5, 1960. 2 figs., 17 refs.

Although the estimation of serum glutamic–oxalacetic transaminase (S.G.O.T.) activity is widely used in the diagnosis of myocardial infarction the usual rise in level sometimes fails to occur, giving false negative results in about 9% of cases. A similar increase in serum lactic dehydrogenase (S.L.D.) activity has often been observed after myocardial infarction.

In a series of 32 patients admitted to the North Lonsdale Hospital, Barrow-in-Furness, with unequivocal evidence of myocardial infarction the present authors found an increase in the S.L.D. level in every case, whereas the S.G.O.T. level was significantly elevated in only 29. In another group consisting of 18 patients with prolonged cardiac pain, but with only T-wave changes in the electrocardiogram, there were 2 in whom the S.L.D. level was not elevated; in these 2 cases and in 3 others the S.G.O.T. level was within normal limits.

The estimation of S.L.D. activity is simpler to carry out than that of S.G.O.T. activity and the elevation of the former after infarction appears to be more prolonged than that of the latter. On the other hand a rise in S.L.D. activity has been observed in various other diseases, such as carcinoma, anaemia, leukaemia, heart failure due to mitral stenosis, femoral venous thrombosis, pneumonia, and cerebral thrombosis. The authors suggest, however, that so long as it is not regarded as a specific test for myocardial infarction the assay of S.L.D. activity may be of considerable value in the investigation of chest pain of cardiac type and to have definite advantages over other enzyme assays.

Z. A. Leitner

989. **Myocardial Infarction Among Members of Communal Settlements in Israel**
D. BRUNNER and G. MANELIS. *Lancet* [*Lancet*] **2**, 1049–1050, Nov. 12, 1960. 9 refs.

The 10-year survey undertaken to examine the influence of physical exercise on the incidence of myocardial infarction, here reported from the Government Hospital, Jaffa, Israel, was carried out on 4,500 men and 4,000 women all working and living in communal settlements (Kibbutzim and Kvutzoth) where the diet and environmental conditions of the inhabitants, irrespective of occupation, are virtually identical. The ages of the subjects at the beginning of the survey (1949) ranged from 30 to 55 years and full medical records were available for all. The incidence of myocardial infarction, as established by the clinical, electrocardiographic, and in fatal cases the post-mortem findings, was then compared in sedentary and non-sedentary workers.

During the period 1949–59 there were in all 111 cases of myocardial infarction, of which 34 were fatal; 19 of these occurred in sedentary workers, while of the 77 non-fatal cases, 42 were in sedentary workers, a total in this group of 61 (55%). Of the 111 cases, only 9 occurred in women, of which 2 were fatal. Since 30% of the population studied were engaged in sedentary work and 70% in non-sedentary work the annual incidence by occupation was calculated to be 1·36 per 1,000 for non-sedentary male workers and 4·1 per 1,000 for sedentary male workers. The authors point out that these results do not support the reputed proneness to ischaemic heart disease of Jewish men, and note that the incidence of myocardial infarction here reported for sedentary workers is almost identical with that reported by Morris *et al.* (*Lancet*, 1953, **2**, 1053 and 1111; *Abstr. Wld Med.*, 1954, **15**, 313) for sedentary workers in London.

H. F. Reichenfeld

HYPERTENSION

990. **Hypertension and Cerebrovascular Disease**
J. MARSHALL. *Lancet* [*Lancet*] **2**, 881–885, Oct. 22, 1960. 9 figs., 11 refs.

In an attempt to throw light on the obscure relation between hypertension and the development of cerebrovascular disease the author, working at the National Hospital, Queen Square, London, has investigated 134 patients (91 men and 43 women) aged 70 years or less, each of whom had suffered an episode clinically diagnosed as non-embolic cerebral infarction. A day in hospital provided the opportunity for clinical observation, the patients remaining supine and their blood pressure being measured every hour for 6 hours. The series did not include any patient with known secondary hypertension.

Study of the systolic blood pressures of the whole group revealed a bimodal distribution, with modes at 112 and 168 mm. Hg. When the systolic pressures of the 82 patients aged 60 and under were plotted separately from those of the 52 over 60 the graph for the latter group showed a pronounced mode at 168 mm. Hg while that for the latter showed a mode at 132 mm. Hg, though both still showed a suggestion of bimodality. The bimodality in the whole group, which was less pronounced for men than for women, was thus shown to be due in part to the inclusion of older patients with high blood pressure (senile hypertension). The systolic pressures of patients under 60 one or both of whose parents had died before reaching the age of 65 also showed a bimodal distribution, but this was not the case when both the parents had survived to 65 or over. On the other hand the systolic pressures of patients over 60, whatever the age of their parents at death, had a bimodal distribution. Similar findings were obtained from a study of the diastolic blood pressures. The data for patients over 60 do not suggest that senile hypertension is related to the age at death of the parents, and there is thus no evidence of a hereditary factor in this type of hypertension. In patients under 60, however, the converse would appear to be true, the group with hypertension being made up entirely of patients whose parents had died before the age of 65.

The author points out that a similar bimodality of blood-pressure distribution has been demonstrated in other groups of subjects and concludes " that the level of blood-pressure cannot be regarded as a feature distributed continuously throughout the population, but that there are different groups, the recognition and study of which will aid our understanding of hypertension and of its relation to cerebrovascular disease ". He considers that it would also be valuable to attempt to correlate the pathological changes found in cerebrovascular disease with these various clinical groupings, though he urges that the study must not be limited to morbid anatomy. He suggests that " dynamic factors in the life-histories of patients " may provide clues to aetiology and lead to better means of managing the disease.

A. C. F. Green

991. **Involuntary Sclerosis and Diastolic Hypertension: Effect of Environmental Change**
A. M. COHEN, E. NEUMANN, and I. C. MICHAELSON. *Lancet* [*Lancet*] **2**, 1050–1051, Nov. 12, 1960. 4 refs.

There is some evidence that arteriosclerotic cardiovascular disease is more prevalent in the Yemenite community who have lived in Israel for a long time than among recent immigrants from the Yemen. The authors, working at the Rothschild–Hadassah University Hospital, Jerusalem, have therefore compared the incidence of hypertension and retinal arteriosclerosis in two such groups; the inquiry was carried out by house-to-house visits of entire settlements, all persons over the age of 30 being included in the survey.

In the first group, which consisted of 70 men and 77 women who had immigrated to Israel during the previous 10 years, hypertension (blood pressure over 140/90 mm. Hg) was noted in 4 males and 13 females, all these except 2 of the women being over 55 years of age. The corresponding figures for retinal involutionary sclerosis were 9 males and 11 females, of whom all but 5 women were over the age of 55.

The 55 men and 70 women in the second group had been resident in Israel for a period of not less than 25 years. In this group 27 males and 29 females with

hypertension were discovered, and of these, 20 men and 21 women were aged over 55. The figures for those with retinal changes were 7 men and 27 women under the age of 55 and 26 men and 33 women over that age. The higher incidence of hypertension and of degenerative vascular changes in the "settled" (second) group is clear, and this is related to the previously reported findings of higher blood cholesterol and phospholipid levels in this group. Also the incidence of diabetes—which is virtually non-existent among the newly arrived Yemenites—in the settled group approached that among Western Jews, and during the course of this survey 9 new cases of the disease were discovered. All these differences are attributed to the great difference in the conditions of life, notably food habits and the general strain of living, as between Israel and the Yemen.

H. F. Reichenfeld

992. **Essential Hypertension. Haemodynamic Observations with a Bearing on Its Pathogenesis**
J. BROD. *Lancet* [*Lancet*] **2**, 773–778, Oct. 8, 1960. 7 figs., 44 refs.

The haemodynamic changes in healthy subjects and in patients with hypertension subjected to pressor stimuli were studied at the Institute for Cardiovascular Research, Prague, Czechoslovakia. With the forearm screened from the patient's sight, thin polyethylene tubes were inserted into the right brachial artery and right antecubital vein, both tubes being connected to three-way stopcocks. A microinfusion of inulin and *p*-aminohippurate was given through the venous tube at a rate of 0·3 ml. a minute. The other tap of the venous stopcock was used for injecting congo red or rose bengal, indicators for the dye-dilution method of estimating cardiac output. The arterial cannula was connected by one tap of the stopcock to a capacitance manometer for direct blood pressure measurement, while the other tap was connected to an apparatus collecting samples every two seconds. The disappearance curve of rose bengal was used as an indicator of splanchnic flow, since 80% of this dye is removed from the blood by the liver. The skin blood flow was assessed by means of a thermocapsule on the right arm, while blood flow through the left forearm was measured by occlusion plethysmography, the difference between these two values being taken as the muscle blood flow. The pressor stimuli applied were a stressful exercise in mental arithmetic (the patient being asked to start with the number 1,194 and subtract 17 every 2 seconds), a verbal suggestion of strenuous exercise (with the eyes closed the patient imagined riding uphill on a bicycle for 10 minutes), and immersion of one leg in cold water (4° C.) for 2 minutes.

These pressor stimuli caused a reduction in the blood flow in the skin and splanchnic area as well as in the kidneys and an increase in forearm muscle flow; the subject, in fact, became ready for strenuous exercise. This effect wore off in healthy subjects in an average of 7·3 minutes. In hypertensives the visceral vasoconstriction was exaggerated, but otherwise the response was similar to that in healthy subjects except that it lasted on the average 29 minutes. The haemodynamics of an acute pressor reaction in normotensives resembles the haemodynamics of hypertensives at rest, with a preponderance of visceral and skin vasoconstriction components over muscular vasodilatation. In essential hypertension, therefore, there is a disturbance of the basic haemodynamic reaction preparing the organism for muscular action. The author notes that social restraints prevent the organism from responding by violent muscular exertion to the pressor stimulus, although the body has prepared it to do so.

G. S. Crockett

993. **Aldosterone Excretion in Essential Hypertension**
J. B. GARST, N. P. SHUMWAY, H. SCHWARTZ, and G. L. FARRELL. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 1351–1359, Oct., 1960. 1 fig., 16 refs.

In a study of the incidence of primary aldosteronism in hypertension, carried out at Crile Veterans Administration Hospital, Cleveland, Ohio, the 24-hour urinary excretion of aldosterone was measured in 18 normotensive patients with no evidence of frank renal, liver, or endocrine disease or of cardiac failure and compared with that in 38 patients with hypertension. No significant difference between the mean excretion rate in the 2 groups was found. However, a few very high values were obtained from the hypertensive patients, suggesting that this group was heterogenous. A χ^2 calculation of the theoretical distribution and the actual values for aldosterone obtained in the hypertensive patients confirmed this suggestion.

Of the 38 hypertensive patients, 9 were shown to have an aldosterone excretion very significantly higher than that of the other 29 patients. Six of the hypertensive patients had a low serum potassium level, but only one of these was from among the patients with a high urinary excretion of aldosterone. The values for serum sodium concentration presented a similar picture. Thus about 25% of the patients with essential hypertension had a high urinary aldosterone level, but they did not exhibit the abnormal serum electrolyte changes which occur in primary aldosteronism.

P. A. Nasmyth

994. **Blood Volume Changes Associated with Essential Hypertension**
D. B. ROCHLIN, T. SHOHL, and W. S. BLAKEMORE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **111**, 569–576, Nov., 1960. 3 figs., 9 refs.

The first part of this paper from the University of Pennsylvania School of Medicine, Philadelphia, reports the results of a comparative study of the blood volume in 16 female and 21 male hypertensive patients and 19 female and 26 male normotensive subjects carefully matched for age, height, weight, and sex. The second part deals with blood volume changes before and after the surgical treatment of hypertension by means of staged bilateral or subtotal adrenalectomy and subdiaphragmatic sympathectomy in 46 patients who had proved refractory to medical treatment. The blood volumes were calculated from the total body haemoglobin mass, which was determined by the method using erythrocytes labelled with radioactive chromium. There was a statistically significant difference between the blood

volume of normotensive and hypertensive patients, the values in the former being 70·0±3·88 ml. per kg. body weight for females and 76·1±4·17 ml. per kg. for males, whereas in the latter they were 61·0±5·28 ml. per kg. for females and 67·5±5·92 ml. per kg. for males.

In the hypertensive patients treated surgically the hypotension which developed during the immediate postoperative period required the transfusion of volumes of blood for the maintenance of a systolic blood pressure of 130 mm. Hg which were larger than the weighed blood loss measured at the time of operation, this being partly due to retroperitoneal haemorrhage. The blood volumes of the operated patients were also observed for a period of 2 months to 3 years after operation. With the exception of 2 cases the blood volume changes were less than 5% of the original blood volume. Finally, no correlation could be found between the patient's blood volume and clinical response to the operation in terms of return to normal blood pressure. The study revealed that in the average normotensive subject the blood volume is some 500 to 700 ml. greater than in the average hypertensive patient of similar physical characteristics, age, and sex. *A. I. Suchett-Kaye*

995. **Treatment of Severe Hypertension with Bretylium Tosylate**

E. F. D. Montuschi, H. E. S. Pearson, and L. L. Wilson. *British Medical Journal* [*Brit. med. J.*] **2**, 1199–1203, Oct. 22, 1960. 14 refs.

In this paper from the Whittington Hospital, London, the authors report the results of treatment of 75 cases of severe hypertension with bretylium tosylate over a period of 9 months. The drug was given at 8-hourly intervals, always before meals to facilitate absorption, in an initial dose of 100 mg., with subsequent increases of 100 mg. 3 times a day every other day, or more if necessary to obtain the desired effect. No other hypotensive agents were given in the initial stages of treatment, but subsequently the oral diuretic hydroflumethiazide was added in many cases. The 75 patients, 38 men and 37 women of an average age of 48 years, who all had a diastolic blood pressure of over 120 mm. Hg, were subdivided into five groups as follows: (1) severe benign hypertension (7 cases); (2) severe benign hypertension with cardiac involvement (39); (3) severe benign hypertension, albuminuria, and a blood urea level greater than 50 mg. per 100 ml. (13 cases); (4) malignant hypertension irrespective of aetiology (13 cases); (5) severe benign hypertension in pregnancy (3 cases). The results of treatment were assessed as satisfactory when the diastolic blood pressure could be lowered to and maintained at around 90 mm. Hg, although in the more severe cases higher diastolic blood pressures were accepted if accompanied by other evidence of improvement. The minimal effective dose for prolonged administration varied from 100 to 1,800 mg. 3 times a day. The adjuvant effect of hydroflumethiazide in a dosage of 100 mg. per day was the most helpful single factor in allowing a greater number of patients to take the optimum dose of the drug without developing side-effects or tolerance.

Successful control of the hypertension over a period of 6 to 9 months was achieved in 53 (71%) of the patients, including 7 of the 13 with malignant hypertension. The drug had to be discontinued in only 9 cases because of side-effects, and the authors consider that this freedom from the more serious side-effects consequent upon parasympathetic blockade is a marked advantage of bretylium tosylate. In their experience the main disadvantage in its clinical use is its variable absorption from the gastro-intestinal tract, resulting in either severe postural hypotension after quite low doses or the necessity for very large doses. They stress, however, that the side-effects resulting from this high dosage can be almost completely avoided by the simultaneous administration of hydroflumethiazide. The principal side-effects were postural hypotension or syncope [in an unstated number of cases], general tiredness, stuffiness of the nose, parotid pain in 25% of the cases, diarrhoea, headaches, and dyspnoea. They found the drug unsuitable for the treatment of moderate benign hypertension in active patients, while its failure to reduce the blood pressure of the recumbent patient makes it ineffective for the treatment of patients confined to bed. In all other cases of hypertension, provided there is no established coronary or cerebral vascular disease, bretylium tosylate represents an important advance in treatment, although its use requires careful supervision. *J. Warwick Buckler*

996. **Detection of Unilateral Renal Disease in Hypertension with Diodrast ^{131}I**

C. T. Dollery. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 969–972, Nov., 1960. 5 figs., 6 refs.

Ideally the counting rate from scintillation detectors directed down at the kidneys after injection of diodone labelled with radioactive iodine (^{131}I) should show: (1) a quick rise due to the passage of labelled blood past the crystal; (2) a slower rise as the radioactive diodone is concentrated within the kidneys; and (3) a fall as the material passes into the urine and out of the field of the counters. Thus variation in corresponding rates between the kidneys should point to malfunction in one or the other. In practice, however, the author found that rates for the right kidney were usually higher than for the left. Investigation in man and experimental animals showed that this was due to liver uptake. Anatomical convergence made it impracticable to reduce the contribution of the liver by improved collimation.

In order to overcome this the fall in the counting rate from the peak was taken as possibly being a more constant measurement. The abdomen was compressed with a cuff for about 10 minutes and then suddenly freed so that the renal pelves emptied rapidly. This technique was successful in about 60% of patients. In the remainder, a third detector showed a leakage into the bladder before compression was released. In general the results indicated that most clear-cut interpretations were possible in patients whose over-all renal function was good, but that where only poor contrast was produced on an intravenous pyelogram the technique became practically useless. *I. M. Rollo*

Clinical Haematology

997. **Hereditary Non-spherocytic Hemolytic Disease**
M. E. CONRAD JR., W. H. CROSBY, and D. L. HOWE. *American Journal of Medicine* [*Amer J. Med.*] **29**, 811–819, Nov., 1960. Bibliography.

Since January, 1955, at the Walter Reed Army Hospital, Washington, the authors have seen 21 cases of " indirect " bilirubinaemia without morphological abnormality of erythrocytes. In only one case was the condition classified as Gilbert's disease (constitutional hepatic dysfunction); in all the others there was non-spherocytic haemolytic disease of varying severity. Some of the patients had anaemia and reticulocytosis, but in others the reduced life span of the erythrocytes could be demonstrated only by measuring the survival of the patient's own erythrocytes transfused after labelling with radioactive chromium. In 11 cases there was a family history of jaundice or cholelithiasis. The response to the Coombs test was always negative and the erythrocyte fragility was within normal limits. The results of liver function tests were normal and there was no increase in conjugated bilirubin. The spleen was palpable in 7 patients, but 4 others had undergone splenectomy without benefit. Jaundice was first recognized in childhood in 6 of the patients; only one was over 40 years old at the time of examination.

[Clearly the differentiation of this disorder from Gilbert's disease may be a matter of extreme difficulty, but clinicians may draw comfort from the fact that both conditions are benign and best treated by masterly inactivity.] *P. C. Reynell*

998. **Blood Transfusion Reactions: Changing Concepts of Etiology. A Promising Means of Prophylaxis and/or Treatment with Intravenous Prednisolone**
F. M. OFFENKRANTZ, A. BLAUSTEIN, and G. BABCOCK JR. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 390–399, Sept.–Oct., 1960. 30 refs.

The value of intravenous prednisolone (" meticortelone soluble ") as a prophylactic agent for blood transfusion reactions was studied in 105 patients who received a total of 436 transfusions. All of the patients represented severe transfusion problems with histories of intractable allergic responses, hemolytic factors, and the presence of iso-agglutinins. The value of intravenous prednisolone as a therapeutic agent for blood transfusion reactions was studied in 17 patients, 5 of whom were erythroblastotic infants. The remaining 12 patients developed severe reactions during postoperative transfusions despite the prior addition of prophylactic antihistamines to the units of blood. No reactions occurred in any of the 105 patients receiving the steroid prophylactically.

Intravenous prednisolone appears to be a safe and highly effective agent for the prophylaxis or treatment of blood transfusion reactions. The steroid exhibited no influence on electrolyte balance. There was no instance of steroid-induced edema or diabetes. Patients with gastrointestinal bleeding who received the drug showed no aggravation of their symptomatology.—[From the authors' summary.]

LEUKAEMIA

999. **The Clinical Significance of Fever in Acute Leukemia**
S. O. RAAB, P. D. HOEPRICH, M. M. WINTROBE, and G. E. CARTWRIGHT. *Blood* [*Blood*] **16**, 1609–1628, Nov., 1960. 10 figs., 12 refs.

Fever in a patient with acute leukaemia may be a manifestation of the leukaemic process itself or of a complication such as haemorrhage or infection. An intensive study is reported of all febrile episodes occurring in patients under treatment for acute leukaemia at Salt Lake County General Hospital, Utah. While routine treatment of the disease was mainly on an outpatient basis, those patients (55) who were markedly febrile were admitted to hospital, when x-ray, particularly of the chest, and clinical examinations were carried out and appropriate specimens were taken for bacteriological and serological investigations.

In these 55 patients 149 febrile episodes occurred, infection being proved in 102 episodes (70%) on the basis of signs of local infection and, usually, the isolation of microbial pathogens. All except 2 of the febrile attacks occurred while the leukaemia was in relapse, and the attacks tended to be more frequent as the duration of the leukaemia increased. Local infection was not usually fatal unless accompanied by blood-stream invasion. The organisms recovered on blood culture in 41 cases were staphylococci in 26 and bacilli of colonic types in 13. Generalized fungus infection occurred in 2 patients; localized forms were not associated with fever. No infection was demonstrated in the remaining 47 febrile episodes. Rectal temperature of 104° F. (40° C.) was usually associated with proved infection, but the height and character of the fever were never completely diagnostic. Moreover, the polymorphonuclear leucocyte count was not helpful.

The authors emphasize the importance of determining the exact organism responsible for infections so that appropriate antibiotic therapy can be given. Bactericidal drugs, such as penicillin and streptomycin in combination, were often administered intravenously even before the results of bacterial culture were available, and adequate antileukaemic therapy such as corticotrophin was given simultaneously.

[Enthusiastic detection and treatment of infections in acute leukaemia, which are not always undertaken, would materially prolong the survival time of a proportion of patients.] *T. B. Begg*

1000. **Leukaemia following Radioiodine Treatment of Thyrotoxicosis**

E. E. POCHIN. *British Medical Journal* [*Brit. med. J.*] **2**, 1545–1550, Nov. 26, 1960. 4 figs., 11 refs.

A study of the incidence of leukaemia following treatment of thyrotoxicosis with radioactive iodine (^{131}I) is reported from University College Hospital, London. A survey of all patients in the United Kingdom known to have been given ^{131}I for thyrotoxicosis showed that leukaemia had developed in 3 out of 10,542 patients treated up to mid-1959. Using the Registrar-General's figures for the incidence of leukaemia according to age and sex in the general population the author estimated that 2·8 cases of leukaemia would have been expected by chance by mid-1960. The incidence of leukaemia was also estimated for the United Kingdom, the United States, Canada, and Austria combined; in these four countries 59,200 patients had been treated by mid-1960. Of these, 21·2 would have been expected to develop leukaemia and 18 are known to have done so. Analysis of the time interval between ^{131}I treatment and the development of leukaemia was also compatible with chance expectation. The proportion of cases of acute leukaemia was higher than expected (13 out of 17) and this is the only point considered to be "suggestive but obviously not conclusive" of leukaemia induction. It is pointed out that total numbers of "patient-years" are increasing rapidly and that many more cases of leukaemia will occur fortuitously during the next few years.

It is suggested that these estimates give no indication that ^{131}I treatment of thyrotoxicosis induces leukaemia.

K. E. Halnan

1001. **Incidence of Leukaemia after Exposure to Diagnostic Radiation *in utero***

W. M. COURT BROWN, R. DOLL, and A. BRADFORD HILL. *British Medical Journal* [*Brit. med. J.*] **2**, 1539–1545, Nov. 26, 1960. 10 refs.

Stewart *et al.* (*Lancet*, 1956, **2**, 447, and *Brit. med. J.*, 1958, **1**, 1495; *Abstr. Wld Med.*, 1956, **20**, 493, and 1958, **24**, 1451) concluded from the results of a retrospective inquiry among mothers whose children had died of malignant disease that in children exposed to x rays *in utero* the risk of dying from cancer before the age of 10 years was approximately double the normal. The present authors, working for the Medical Research Council, report the results of an investigation into the same question by a different technique. Women who had undergone radiography of the abdomen or pelvis during pregnancy between 1945 and 1956, totalling 43,742, were identified in the radiological records of 8 hospitals, 4 in Edinburgh and 4 in North-West London. Most of these women were delivered in, or under the care of, the same or an associated hospital and in as many cases as possible details of the birth were obtained from the maternity records, while the registration of babies born alive was identified in the local or central Register of Births. In this way adequate information was obtained about 39,166 liveborn children who had been irradiated *in utero*. Nine of these infants were identified in a list, provided by the Registrar-General, of the names of children who had died of leukaemia in Great Britain during 1945–58. The expected number, calculated from the death rates for leukaemia for each sex and for each year of life for each calendar year during this period, was 10·5. The observed and expected numbers of deaths from leukaemia among children classified according to age, sex, type of irradiation, and place of residence were closely similar in each case. There was no evidence of any disproportionate occurrence of leukaemia among those children who had been most heavily irradiated or among children who had been irradiated early in intrauterine life. An incidental observation was that the ratio of males to females among the irradiated children (1·15:1) was substantially higher than normal (1·06:1).

The results are discussed and compared with those of similar investigations, the suggestion being made that data based on information obtained from mothers "is likely to be of variable accuracy". It is concluded "that an increase of leukaemia among children due to radiographic examination of their mother's abdomen during the relevant pregnancy is not established".

A. Ackroyd

1002. **Leukaemia in Childhood after Antenatal Exposure to X Rays: a Survey at Queen Charlotte's Hospital**

T. L. T. LEWIS. *British Medical Journal* [*Brit. med. J.*] **2**, 1551–1552, Nov. 26, 1960. 3 refs.

It was concluded by Stewart *et al.* [see Abstract 1001] that although leukaemia was more frequent in children who had been irradiated *in utero*, such irradiation could not have been the cause of leukaemia in childhood in more than 6% of cases or in more than 1 in 40,000 births.

To test the validity of this argument an investigation was undertaken into the incidence of leukaemia in children born at Queen Charlotte's Hospital, London, where about 25% of all pregnant mothers undergo an obstetric abdominal x-ray examination compared with an estimated national average of 16%. The hospital records for the period 1943–58 were searched to see whether any of the 1,548 children who died of leukaemia in England and Wales before their tenth birthday during the 6 years 1953–8 had been born in the hospital. In 26 instances the name of an infant born at Queen Charlotte's in the appropriate year was similar to that of one who had died of leukaemia, but examination of the birth and death certificates proved that only 8 were in fact identical. (Allowing for errors in the method, the number might be 10). Among the 45,195 live births at the hospital during the 16-year period the expected number of deaths from leukaemia, as calculated from the known mortality in each age group, would be 6·6. But although 11,433 foetuses had been irradiated during that period, this total included only one of the 8 children who were known subsequently to have died of leukaemia. Calculations show that 1 in 1,808 babies who were not irradiated died of leukaemia compared with 1 in 4,291 of those who were, the total incidence of the disease among children born at the hospital being 1 in 2,118 (national incidence 1 in 2,600). It is concluded that "although the figures are not large enough to show a tendency for irradiation of the foetus to cause one case of leukaemia in 40,000 births, they do show that the tendency is not very much greater."

A. Ackroyd

Respiratory System

1003. **A Study of Essential Hemoptysis**
R. J. BARRETT and W. M. TUTTLE. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] 40, 468–474, Oct., 1960. 11 refs.

The authors of this paper from the Harper and Detroit Memorial Hospitals, Detroit, report a study of 97 cases of haemoptysis of undetermined origin seen between January, 1950, and April, 1959. At the initial examination all the patients were subjected to bronchoscopy and bronchography and bronchial aspirate was obtained for culture. The results of these investigations were [needless to say] negative. Of the 97 patients, 81 were followed up after one to 9 years; 4 had died from causes unrelated to the haemoptysis and the remaining 77 were known to be alive. In none of the cases did pulmonary tuberculosis or carcinoma of the bronchus develop. Nevertheless, the authors recommend that serial radiographs should be taken in such cases for at least one year after the initial examination. They state in conclusion that the majority of patients "will continue in good health even though over 10% may continue to have occasional episodes of hemoptysis. In an analogous situation in the urinary tract, with the same prognosis, the term 'essential hematuria' is widely accepted . . . there is equal evidence to support the terminology of 'essential hemoptysis'" in the cases described.

(In the subsequent discussion the importance of parasitic lung infection, especially with *Paragonimus westermani*, was emphasized; the chest radiograph in such cases may be quite normal in the initial stages. Broncholiths due to histoplasmosis may also cause spitting of blood and not uncommonly the patient gives a history of coughing up "stones".) *Paul B. Woolley*

1004. **Experimental Effect of Cigarette Smoke on Human Respiratory Cilia**
J. J. BALLENGER. *New England Journal of Medicine* [*New Engl. J. Med.*] 263, 832–835, Oct. 27, 1960. 3 figs., 24 refs.

The effect of cigarette smoke on human respiratory cilia was investigated in small areas of epithelium obtained from the posterior pharynx of children under general anaesthesia for respiratory operations at Evanston Hospital, Illinois.

The activity of the cilia in these collections of cells was noted by movement of the cells in a rotary direction observed by intermittent photography when the isolated tissue was suspended in nutrient solutions. The collection of cells rotated rapidly until a solution of similar *p*H containing smoked basic salt solution was perfused through the preparation; rotation of the cells then ceased and they disintegrated. The observations suggest that smoking results in a decreased efficiency of the respiratory cilia and increased local exposure to carcinogenic substances. *J. Robertson Sinton*

1005. **Minor Disease in Ten "Healthy" Adults: an Intensive, Day-by-day, Clinical and Virologic Study**
M. J. MCNAMARA, E. H. THOMAS, A. STROBL, and E. D. KILBOURNE. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] 82, 469–481, Oct., 1960. 25 refs.

This paper from Cornell University Medical College, New York, describes a study undertaken to assess the frequency of morbidity due to minor respiratory illness in a small group of adults. Ten laboratory workers (5 men aged 30 to 51 and 5 unmarried women aged 26 to 43) had their symptoms (or the lack of them) recorded daily for 266 days under such headings as "Eye", "Ear", "Nasal", "Mouth", "Throat", "Neck" (pain, stiffness, swollen lymph nodes), "Chest" (pain, cough, shortness of breath), "Cardiac" (palpitations), "Abdomen" (pain, diarrhoea, nausea, vomiting, and anorexia), "Genitalia", "Skin", "Musculo-skeletal" (back pain, myalgia, arthralgia), and so forth. Temperature was recorded morning and evening. Currently recognized laboratory techniques were employed to isolate adenoviruses, para-influenza virus Types 1 and 3, Group-B Coxsackie viruses, and the herpes simplex virus from thrice-weekly pharyngeal swabs. In addition, complement-fixation tests for influenza A and B viruses, the Asian strain (Jap. 305), and B/G1/54 strain were also carried out. Bacteriology was not explored.

The average number of symptom-free days per person was 120 of the 266, though the extremes of the percentage of symptom-free days varied from 6% to 78%. Symptoms were recorded from September to the following May, and the "symptom incidence" was found constant in each individual. Slightly less than 50% of all symptoms referred to the respiratory tract, and although gastro-intestinal symptoms constituted only 6% of all symptoms, they were the next most troublesome "in contributing to specific illness and absenteeism". Symptoms involving other systems were usually associated with respiratory and gastro-intestinal symptoms or were isolated and transient. Of localized symptoms, the commonest in order of "percentage incidence" were: sore throat; nasal congestion; non-productive cough; myalgia; "burning" eyes or retro-orbital pain; laryngitis (hoarseness of voice); chest pain related to coughing; anorexia, nausea, and/or vomiting; swollen cervical lymph nodes; and, finally, recurrent herpes simplex of the lips.

Of 439 throat and 11 rectal swabs (75 of the former and all of the latter taken during overt illness), none revealed the presence of "cytopathic agents", and serological studies gave only 2 positive results—one a complement-fixing and haemagglutination-inhibiting antibody to influenza B virus, and the other an adenovirus infection.

The authors comment upon the high frequency of minor symptoms described and of the need to observe these against the "background" of symptoms which individuals may habitually suffer; for example, an indi-

vidual with chronic sinusitis frequently suffered exacerbations of this following acute respiratory illness. The failure to identify organisms responsible for these minor illnesses was thought to be due to the present inadequacy of the available laboratory techniques.

[There appears to be much scope for extended work of this order. It is the abstracter's impression that " minor illnesses " of the respiratory and gastro-intestinal tracts have become more common in recent years.]

W. Raymond Parkes

LUNGS AND BRONCHI

1006. **On the Relations between Atmospheric Pollution in Urban and Rural Localities and Mortality from Cancer, Bronchitis and Pneumonia, with Particular Reference to 3:4 Benzopyrene, Beryllium, Molybdenum, Vanadium and Arsenic**

P. Stocks. *British Journal of Cancer* [*Brit. J. Cancer*] 14, 397–418, Sept. [received Nov.], 1960. 10 refs.

In this paper a statistical correlation is made between mortality from cancer, bronchitis, and pneumonia and measurements of atmospheric pollution in representative locations in North Wales, Lancashire, Yorkshire, and Tyneside. The methods used for estimating the amount of smoke and polycyclic hydrocarbons (3:4-benzopyrene, 1:12-benzoperylene, pyrene, and fluoranthene) are described and the problems encountered are discussed. To reduce variability to the minimum mortality figures for cancer of the lung for 1950–4 and for the other diseases for 1950–3 were used, the atmospheric pollution measurements being recorded during the period 1955–8. The significance of error due to the use of a single site for such measurements is mentioned and it is recommended that more than one should be used in districts with a population of more than 50,000.

The mean annual concentration of smoke in the various locations was found to range from 15 to 562 mg. per 1,000 c.m., of 3:4-benzopyrene from 1 to 108 mg. per 1,000 c.m., of 1:12-benzoperylene from 0·4 to 74 mg. per 1,000 c.m., of pyrene from 1 to 38 mg. per 1,000 c.m., and of fluoranthene from 3 to 58 mg. per 1,000 c.m. The standardized mortality ratios (taking mortality in England and Wales as 100) for lung cancer ranged from 23 to 165, for other cancer from 68 to 122, for bronchitis from 18 to 259, and for pneumonia from 61 to 227

The findings are summarized as follows. " Lung cancer mortality is strongly correlated with smoke density in the atmosphere in 26 areas in Northern England and Wales, in 45 districts of Lancashire and the West Riding of Yorkshire, and in 30 county boroughs, whilst similar though weaker correlations are found within Greater London. These relations are only partially explicable by social differences in the populations concerned. Bronchitis and pneumonia in males and bronchitis also in females show similar strong correlations with smoke. Cancers of the stomach and intestine are related significantly with smoke in the county boroughs, and cancers of sites other than lung and stomach in males are so related in the other groups of areas. In females cancers of the breast and other organs show no association with smoke. Pollution by larger particles is related significantly with lung and stomach cancers, bronchitis and pneumonia in 53 county boroughs and with lung cancer and bronchitis in 74 districts of Lancashire and the West Riding. In the 26 localities the smoke samples were analysed in respect of polycyclic hydrocarbons and a statistical process of successive elimination was applied to discover which hydrocarbon was responsible for the smoke correlation with mortality rates. For lung cancer and bronchitis 3:4 benzopyrene emerges clearly as the substance of prime importance, with 1:12 benzoperylene contributing weakly for lung cancer, but for pneumonia 3:4 benzopyrene is apparently not important. The composite group of other cancers in males is correlated with several hydrocarbons, but cancers of the breast and other sites in females show no relations with any of them. In 23 localities spectrographic analyses for 13 trace elements were made and a similar process of successive elimination was applied to those which showed appreciable correlations with mortality rates. For lung cancer beryllium and molybdenum emerge as the elements of most consequence, with arsenic, zinc and vanadium showing weaker associations. For bronchitis molybdenum appears to be the important element in both sexes whilst in males beryllium, arsenic, vanadium and zinc may also be concerned as for lung cancer. For pneumonia beryllium emerges as the important element in both sexes, with vanadium also concerned in males. With other cancer in males beryllium, molybdenum and vanadium show associations, but breast and other cancers in females show no relations with any element."

[There is a wealth of detailed information of great value to anyone working in this sphere.]

Kurt Schwarz

1007. **Bullous Emphysema. A Long-term Study of the Natural History and the Effects of Therapy**

D. J. Stone, A. Schwartz, and J. A. Feltman. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] 82, 493–507, Oct., 1960. 3 figs., 14 refs.

The authors believe that " emphasis on physiologic abnormalities provides the most realistic approach to clinical problems ", and they have applied this axiom to the investigation of their cases of bullous emphysema at the Veterans Administration Hospital, Bronx, New York. The study covered 15 males aged between 23 and 45, selected because their chest radiographs suggested bullous formation. These patients were subjected to clinical examination, fluoroscopy and inspiratory and expiratory postero-anterior radiography of the chest, blood counts, electrocardiography, and sputum culture at intervals of 6 to 12 months. Standard pulmonary function tests (lung volume, maximal breathing capacity, ventilation at rest and with exercise, and gas-exchange studies) were carried out in all but one case. In addition, venous angiocardiography was performed before and after operation in 8 cases and bronchography in 4.

The results of these observations, which are presented in detail, suggest that bullous emphysema is " an acquired disease due to imperfect communication between bronchioles and alveolar spaces ". Considerable atten-

tion is paid to the nature of bullae, their bronchiolar connexions and check-valve mechanisms. The authors recommend long-term observation, as this has revealed discrepancy between symptoms and the extent of bullous emphysema which may be due to bronchitis of varying severity.

The pulmonary function studies revealed that ventilatory insufficiency and hyperventilation are the most constant findings. Significant, though relatively slight, defect in gas exchange may accompany large air-trapping bullae, but " greater abnormalities are undoubtedly due to generalized bronchitis or obstructive emphysema ".

In some patients serial observations suggested that medical treatment (antimicrobial and antispasmodic) may lead to improvement; it was a useful adjunct in cases treated surgically.

The authors believe that the only common denominator to be used as a criterion for surgical excision of bullae is the demonstration of abnormal air-trapping reflected in the lung function tests noted. The patient to be expected to benefit most from surgery is the young person with progressive enlargement of air-trapping bullae who has little or no bronchitis and no clinical or functional evidence of generalized emphysema. The least likely candidate is the older patient in whom clinical and functional evidence indicates generalized obstructive emphysema in which " the bulla is, in reality, nothing more than a chance roentgenographic finding "; these patients are best treated medically. Most patients, however, do not fall neatly into these categories, and in those with enlarging bullae, bronchitis, and " varying degrees of ventilatory and alveolorespiratory insufficiency " no general indications for surgery can be laid down.

[This is a fairly detailed paper, and those interested should read it in full.] *W. Raymond Parkes*

1008. **Demographic Approach to the Problem of the Connexion between Lung Cancer and Smoking**

J. R. RELE. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 181–184, Oct., 1960. 4 refs.

Since the city of Bombay contains an ethnic group of some 70,000 Parsees who differ from the remaining 3,500,000 of the population in that, on religious grounds, they do not smoke, and since it also has an excellent system of registration of births and deaths in the city, complete with certified causes of death, it offers a fruitful ground for investigating the connexion between smoking habits and cancer of the lung. In such a study the author established that in the years 1957 and 1958 there were 63 male and 76 female deaths from cancer (all sites) among the Parsees and 1,007 male and 519 female similar deaths among non-Parsees, giving crude cancer death rates (per 100,000 per annum) for males of 90 in Parsees and 23 in the rest and for females 109 and 20 respectively. Since the Parsee community enjoys a higher standard of living and thus a greater expectation of life these rates were standardized for Parsee age distribution, whereupon the above rates for males became Parsees 90 and the rest 81, and those for females 109 and 53 respectively. When the deaths from lung cancer were calculated as percentages of all cancer deaths, the figures were 3·2 for male Parsees and 12·5 for male non-Parsees, and for females 2·6 and 3·5 respectively; thus the percentage of deaths from lung cancer was significantly higher in male non-Parsees than in the three (generally) non-smoking categories of male and female Parsees and female non-Parsees. The author concludes that the relatively low risk of lung cancer in male Parsees is probably related to the fact that they do not smoke. *F. T. H. Wood*

1009. **The Diagnostic Value of Pleural Biopsy in Bronchopulmonary Carcinoma**

W. PAGEL and S. GOLDFARB. *Journal of Clinical Pathology* [*J. clin. Path.*] **13**, 425–431, Sept., 1960. 18 figs., 10 refs.

The value of pleural biopsy in the diagnosis of bronchopulmonary carcinoma was assessed from the findings in 26 patients subjected to this procedure at Clare Hall Hospital, South Mimms, Hertfordshire, biopsy being performed with either the Adams or the Harefield needle. Carcinoma was diagnosed from the pleural biopsy specimen in 13 of the cases, this diagnosis being confirmed by bronchial biopsy, by the findings on bronchoscopy, or by examination of pleural fluid and sputum for neoplastic cells. In the remaining 13 cases there was no evidence of carcinoma in the pleural biopsy specimen; nevertheless carcinoma was present in 7 of them. Pleural biopsy also revealed in this series one case of tuberculosis and one case suggestive of a rheumatic aetiology, the microscopical appearances being reminiscent of those seen in the cellular parts of rheumatic infiltrates. In all the positive cases a real infiltration of the pleural membrane by neoplastic cells was demonstrated.

The authors suggest that pleural biopsy can be of value in corroborating the diagnosis of carcinoma arrived at by other means, rendering bronchial biopsy unnecessary and providing a positive result in those cases in which the findings on bronchial biopsy are negative. They state that a point of interest is the comparatively frequent presence of deposits in the parietal as opposed to the visceral pleura, a finding which is worthy of further study. *G. Clayton*

1010. **The Erythrocyte Sedimentation Rate in Carcinoma of the Bronchus**

B. P. HARROLD and P. R. SLADE. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **55**, 1–5, Jan., 1961. 2 refs.

The erythrocyte sedimentation rate [E.S.R.] has been studied in a series of 301 cases of carcinoma of the bronchus. The E.S.R. was found to be raised in 82·6% of these cases. In adenocarcinomata the E.S.R. was normal in 37·5% of cases. With a normal E.S.R. the growth was confined to the lung or to the lung plus intrapulmonary nodes in 57·7% of cases. The E.S.R. was not considered to be of much help in the differential diagnosis of cases of carcinoma of the bronchus. The level of E.S.R. was not reliable in estimating the prognosis of carcinoma of the bronchus. The E.S.R. is an investigation which appears to have very little value in this disease.—[Authors' summary.]

Urogenital System

1011. **I^{131}-Diodrast Studies in Unilateral Renal Disease**
J. B. BLOCK, G. J. HINE, and B. A. BURROWS. *Circulation* [*Circulation*] **22**, 913–926, Nov., 1960. 12 figs., 16 refs.

From Boston University School of Medicine the authors describe the use of diodone labelled with radioactive iodine (^{131}I) in the diagnosis of unilateral renal disease. The technique used involved the intravenous administration of 300 ml. of a 5% solution of dextrose containing 1 g. of diodone, the injection into the tubing of 2·5 ml. of 35% diodone solution, followed immediately by the rapid injection of 20 μc. of ^{131}I-labelled diodone (about 0·1 mg.) and the simultaneous measurement of radioactivity in the two renal areas by collimated scintillation counters. A recorder was used which showed two tracings, namely, the radioactivity over one kidney and the ratio of the counting rate in this kidney to the total counting rate from both kidneys (the " ratiometer " tracing).

In all, 226 patients were investigated both by this method and by intravenous pyelography, 49 of them also being studied by retrograde ureteral catheterization, while 40 were later subjected to surgical exploration. Some of the typical tracings obtained are reproduced and discussed in detail, the technique providing evidence of the rate of secretion and excretion of the labelled diodone.

The results obtained by this method are compared with those of pyelography, of estimation of sodium concentration and volume of urine obtained by retrograde catheterization (the " Howard test "), and with the surgical findings. The ^{131}I-diodone method was found to be extremely useful in detecting slight differences in function between the two kidneys and in this respect also correlated well with the surgical or post-mortem findings. It is noted that an abnormal ^{131}I-diodone tracing is obtained when the urine flow from the two kidneys differs; thus in 3 patients with unilateral renal arterial stenosis the intravenous pyelogram was normal, but the ^{131}I-diodone tracing was abnormal. *K. E. Halnan*

1012. **Epidemiology of Urinary-tract Infections: a Pilot Study of 3057 School Children**
C. M. KUNIN, I. SOUTHALL, and A. J. PAQUIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 817–823, Oct. 27, 1960. 1 fig., 21 refs.

The authors, from the University of Virginia School of Medicine, Charlottesville, describe their findings in a survey of the incidence of urinary-tract infections in 3,057 school-children in Waynesboro, Virginia. A total of 1,647 boys and 1,410 girls, constituting 85% of the children enrolled in the city schools, participated. Morning specimens of urine were collected without special preparation from the boys and after cleansing of the external genitalia from the girls.

Only 15 of the 1,647 specimens of urine from the boys showed growth of organisms, and subsequent specimens were either sterile or contained fewer than 1,000 colonies per ml. On the other hand 203 (14·4%) of the specimens from the girls contained 50,000 or more colonies of bacteria per ml. After a more careful swabbing of the genitalia a second specimen was produced by these 203 girls; 58 still contained at least this number of colonies, 35 having more than 100,000 colonies per ml. These girls were then catheterized [the ethics of this seem questionable]; all those who previously had fewer than 100,000 colonies per ml. now had a negative culture, but 15 (42·9%) of the 35 with more than 100,000 colonies per ml. had a positive culture, usually of *Escherichia coli*; 5 of them also had more than 4 pus cells per high-power field. Two of these 15 girls had had previous treatment for known infection of the urinary tract, but in the remainder such infection was unsuspected. The prevalence of infection in the girls was thus roughly 1%. A history of minor symptoms of infection, especially of the lower urinary tract, was given by 13 of the 15 girls. In 5 cases cystograms were abnormal, with probable reflux in 4. One child had hydronephrosis and hydro-ureter, in 2 the renal pelvis was reduplicated, one showed blunting of certain calyces, and in one there was slight ptosis of a kidney.

Of the total of 3,057 children, 290 (9·5%) had 30 to 300 mg. of protein per 100 ml. of urine, but only 2·8% were regarded as having significant proteinuria. Only 4 children (0·13%) had significant glycosuria.

The authors conclude that minor and often undiagnosed urinary infections are fairly common in girls, and that their importance in chronic pyelonephritis needs further study.

[An interesting and original study.] *Arnold Pines*

1013. **Prophylactic Hemodialysis in the Treatment of Acute Renal Failure**
P. E. TESCHAN, C. R. BAXTER, T. F. O'BRIEN, J. N. FREYHOF, and W. H. HALL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **53**, 992–1016, Nov., 1960. 10 figs., 40 refs.

The authors, at Brooke Army Medical Center, Fort Sam Houston, Texas, have carried out prophylactic haemodialysis on 15 patients with acute renal failure in order to keep the blood non-protein nitrogen level below about 150 mg. per 100 ml. and thereby prevent the development of the uraemic syndrome and its commonly lethal sequelae.

There were 12 patients with acute tubular necrosis (6 post-traumatic), 2 with bilateral renal cortical necrosis, and one with acute glomerulonephritis. In all, in 398 days of oliguria 193 dialyses were performed. Repeated dialysis was simplified by keeping plastic arterial and venous cannulae in place between dialyses, and when

necessary regional extracorporeal heparinization was used. Contamination of the cannulae with organisms, especially *Aerobacteror klebsiella*, was common, and this probably accounted for the frequency of rigors and fever soon after the onset of dialysis. There was remarkable freedom from uraemic symptoms and infections, and wound healing was good. Use of combined ultrafiltration and dialysis allowed the patients to have a liberal fluid intake, and their dietary regimen was also liberal. Anaemia and reticulocytosis were seen frequently in the oliguric phase. The 2 patients with cortical necrosis died after 73 and 92 days of oliguria, having had 29 and 40 dialyses respectively. There were 3 deaths among the patients with acute tubular necrosis—one unexplained, on the 26th day, one due to cerebral haemorrhage, and one due to aspiration pneumonia. The authors suggest that prophylactic dialysis may become standard practice in large centres for the treatment of acute renal failure.

K. G. Lowe

1014. **Optimal Perfusion-rate in Haemodialysis Combined with Ultrafiltration**

E. E. Twiss and M. M. P. Paulssen. *Lancet* [*Lancet*] **2**, 1055–1056, Nov. 12, 1960. 4 figs.

If progressive uraemia due to acute renal insufficiency is complicated by severe overhydration, treatment with combined haemodialysis and ultrafiltration is indicated. This can be carried out with the Alwall type of artificial kidney by using a higher perfusion rate and increasing the resistance in the circuit by constricting the outflow tube. A metal "skeleton" must also be provided to support the perforated metal cylinders which form the screens for the "cellophane" spiral. In this paper from St. Clara Hospital, Rotterdam, the authors report their experience of ultrafiltration with an Alwall dialyser modified in this way, blood being pumped from the patient by a "sigma" finger pump with adjustable speed. If the rate of flow through the apparatus is too high, excessive pressure inside the coil may lead to its rupture; if too low, the blood becomes excessively concentrated. A flow rate of 10 to 12 litres per hour was found to be optimal, allowing the removal of 300 ml. of fluid per hour. Rates in excess of this led to shock and hypotension. For dialysis without filtration the outflow from the coil is unimpeded and a higher flow rate (20 to 30 litres per hour) is then preferable to ensure rapid dialysis.

[For practical details the original paper should be consulted.] *D. A. K. Black*

1015. **Oliguric Renal Failure of Surgical Origin**

R. Shackman, M. D. Milne, and N. W. Struthers. *British Medical Journal* [*Brit. med. J.*] **2**, 1473–1482, Nov. 19, 1960. 4 figs., 27 refs.

This paper from the Postgraduate Medical School of London, Hammersmith Hospital, summarizes the experience gained in the management of 106 patients with oliguric renal failure complicating surgical and traumatic conditions. The mortality was much higher than in patients with acute renal failure due to medical or obstetric conditions, the survival rate being only about 20%. However, the over-all mortality figure is not very significant in so varied a series of patients, many of whom died from causes other than renal failure. The rate of progression of uraemia was much more rapid than in medical cases, because of increased tissue catabolism, and infection was the most serious hazard. Multiple dialysis was called for in many cases. In about one-quarter of the patients, however, post-renal obstruction was the cause of the oliguria and most of this group survived without the use of dialysis.

[This paper should be read in full by those responsible for the management of acute renal failure; it shows very clearly the range of conditions referred to any team equipped with an artificial kidney.] *D. A. K. Black*

1016. **Acetazolamide-induced Renal Stone.** [A Case Report]

A. R. Mackenzie. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **84**, 453–455, Sept., 1960. 18 refs.

1017. **Treatment of Bladder Tumours**

J. C. Anderson. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 741–748, Sept., 1960. 1 fig., 1 ref.

The author reviews experience in the treatment of carcinoma of the bladder with reference to 778 cases personally assessed and treated between 1947 and 1958, only 5 of which were recognized industrial cases. He states that he has been impressed with the accuracy of clinical and cystoscopic assessment, such assessment in some cases being more accurate than that based on direct inspection of the open bladder. Diagnosis was particularly difficult in cases of intramural spread of carcinoma. In some cases there was difficulty in differentiating between carcinoma and tuberculosis. Cytological examination of the urinary deposit was valuable. In 95 patients there was primary carcinoma at sites other than the genito-urinary tract, the commonest being the lung; in 5 patients there were three primary sites of carcinoma.

Clinical and histological staging of the tumours were in fair agreement. In treatment, superficial lesions were controlled by cystoscopic diathermy for as long as possible, followed by excision combined with interstitial irradiation. If this was not possible high-voltage irradiation was given from an external source or, finally, diversion of urine and cystectomy were carried out. Of those patients dying from other diseases whose bladder condition was known at the time of death, 10% had persisting disease in the bladder.

The author analyses his results in great detail and produces evidence in support of his view that high-voltage irradiation can be of value when other methods of treatment have nothing to offer. Although the majority of patients had Stage-III or Stage-IV disease when first seen and 70% had solid tumours, more than one-third survived 2 years or longer or died from unrelated causes free from bladder disease. Cystectomy secondary to irradiation gave much better results than primary cystectomy. [All those interested in the subject should read this important article in the original.] *K. G. Lowe*

Endocrinology

1018. **Fatal Myxedema, with and without Coma**
J. F. NICKERSON, S. R. HILL JR., J. H. MCNEIL, and S. B. BARKER. *Annals of Internal Medicine* [*Ann. intern. Med*]. 53, 475–493, Sept. [received Nov.], 1960. 2 figs., 47 refs.

In this paper from the University Hospital, Birmingham, Alabama, the authors describe 5 cases (all in females) of severe hypothyroidism, in 4 of which death occurred before there was any response to replacement therapy (parenteral triiodothyronine in a dosage of 30 μg. daily); the remaining patient, who was in semi-coma, made a remarkable recovery with treatment. The authors point out that the signs and symptoms characteristic of severe myxoedema are insidious in onset and progression. Early recognition of the condition is essential and replacement therapy with thyroid hormone should be instituted before the discouraging late clinical picture appears. The beneficial value of glucocorticoids and heat in myxoedema " has not been clearly demonstrated. Their use is rational, and they should be continued until there are definite contraindications ". *G. B. West*

1019. **Hyperuricemia in Myxedema**
R. D. LEEPER, R. S. BENUA, J. L. BRENER, and R. W. RAWSON. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] 20, 1457–1466, Nov., 1960. 5 figs., 11 refs.

During the course of other investigations at the Memorial Center, New York, hyperuricaemia was noted in some patients suffering from myxoedema, and the present study was undertaken to investigate this further. Serum and urinary urate levels were measured by means of Archibald's adaptation of the Kern and Stransky method, and in most cases blood urea concentration was also estimated. Serum uric acid levels were estimated in 28 patients, 16 female and 12 male, with myxoedema diagnosed clinically and confirmed by laboratory tests, while 33 hospital employees served as controls. Urinary urate excretion was determined and the excretion rates were calculated in 6 females and 5 males with myxoedema, and 5 of these patients were studied before and during therapy with either triiodothyronine or triiodothyropropionic acid. Similar studies were also made on 7 hyperthyroid patients.

The mean serum uric acid level for healthy males was 5·2±0·7 mg. per 100 ml. and for healthy females 4·2±0·7 mg. per 100 ml. The mean level in the myxoedematous males was 7·2 mg. per 100 ml. and in the females 4·8 mg. per 100 ml., only 6 of the 16 females having a level higher than 5 mg. per 100 ml. All 6 were post-menopausal. The urinary excretion rate of urate measured in the 11 myxoedematous subjects, not necessarily suffering from hyperuricaemia, was decreased. When triiodothyronine or triiodothyropropionic acid was given in sufficient dosage to raise the basal metabolic rate to normal there was urinary urate diuresis with an increase in 24-hour urate excretion and a fall in serum uric acid level. The 7 hyperthyroid patients showed, if anything, slightly increased excretion of urates.

The findings suggest the existence of a relationship between thyroid function and uric acid metabolism or excretion in the human being and that this effect is mediated primarily through an effect on the kidney, although there is a possibility that the larger doses of thyroid may increase purine turnover rates.

B. M. Ansell

1020. **The Triiodothyronine Suppression Test for Thyrotoxicosis**
W. H. HOATHER and E. J. S. WOOLLEY. *British Journal of Radiology* [*Brit. J. Radiol.*] 33, 701–705, Nov., 1960. 3 figs., 5 refs.

The authors describe their experience with the triiodothyronine suppression test in the diagnosis of thyrotoxicosis. The uptake of radioactive iodine (^{131}I) by the thyroid gland was first estimated at 6, 24, 30, and 48 hours after administration of 20 μc. of the isotope by mouth, and at 48 hours the total plasma activity and the protein-bound fraction were also determined. These measurements were then repeated on the last day of an 8-day course of sodium L-triiodothyronine in a dosage of 30 μg. three times a day, a dosage which did not cause any significant symptoms.

The test has been performed at Derbyshire Royal Infirmary, Derby, as a routine when the results of estimating the initial uptake of ^{131}I by the thyroid gland, the total plasma activity, and the protein-bound fraction are equivocal. A difference of more than 15% between the initial uptake and the post-triiodothyronine 24-hour uptake is regarded as normal, but a difference of 10% or less is considered to be diagnostic of thyrotoxicosis. The results obtained in 46 cases (28 normal and 18 toxic) are summarized in a table. The authors discuss the reasons for anomalous findings. They consider that the results of the triiodothyronine suppression test permit a correct diagnosis in over 95% of cases, whereas those of any other individual test using ^{131}I are correct in less than 60% of cases. *K. E. Halnan*

1021. **Treatment of Goiter and Thyroid Nodules with Thyroid**
E. B. ASTWOOD, C. E. CASSIDY, and G. D. AURBACH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 174, 459–464, Oct. 1, 1960. 20 refs.

An analysis is presented of 230 patients with simple goitre (out of a much larger number) who were observed at the Pratt Clinic–New England Center Hospital, Boston, for periods of several months or years between 1945 and 1958. With the object of reducing the size of the goitre all the patients were given thyroid extract in a dosage of 180 mg. daily. Only 16% had symptoms of thyroid intoxication, these symptoms rarely being severe enough to necessitate a reduction in the dosage.

The size of the thyroid gland returned to normal in almost one-third of the cases, while some regression was

noted in a further one-third. The physical characters, including the size of the goitre, did not influence the response, except that large generalized goitres rarely showed any decrease in size. Surprisingly, the length of time the goitre had been present was also unrelated to the degree of improvement. The longer the patients had been treated, the more satisfactory the results appeared to be. From tests carried out on 51 patients during treatment it appeared that significant regression of the goitre was, to some extent, related to the adequate suppression of the uptake of radioactive iodine by the gland. Furthermore, an increase in the daily dosage of thyroid above 180 mg. led to further reduction in the size of the goitre in 7 of 18 patients whose response was incomplete. Prolonged observation after the end of treatment was not often possible, but it appeared that relapse occurred in over half the cases during the subsequent 2 years. Of 36 patients who were considered on clinical grounds to be hypothyroid, complete regression occurred in 21; there was no response in 7 only. [If these 36 patients are excluded from the general analysis, complete regression occurred in under one-quarter of the cases.]

During the whole period of this study no further increase in the size of a goitre or of an individual thyroid nodule was observed after adequate thyroid treatment had been instituted. The authors consider that this observation should help to lessen the exaggerated fear that thyroid cancer often complicates simple goitre—a view which leads to unnecessary thyroidectomy in many cases. The results of this study suggest that all cases of simple goitre should be treated with thyroid extract, usually in a dosage of at least 180 mg. daily, for a period of a year and probably longer. *H.-J. B. Galbraith*

1022. **The Potentiation of the Action of Insulin by Tolbutamide.** (Über die Verstärkung der Wirkung von Insulin durch Tolbutamid)
A. LINKE. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 2069–2073, Nov. 18, 1960. 6 figs., bibliography.

Writing from the University Medical Clinic, Heidelberg, the author recalls that the various theories put forward to explain the mode of action of the sulphonylureas in carbohydrate metabolism have included (1) an extrapancreatic action through a sedative effect on the β cells; (2) inhibition of the function of the α cells; (3) inhibition of the splitting up of insulin; and (4) promotion of an increased secretion of insulin. He also recalls the well-known experimental results obtained in pancreatectomized animals and those rendered diabetic by the administration of alloxan, which showed that in the absence of insulin the sulphonylureas are ineffective. The author then describes at some length his own experiments with the sulphonylurea tolbutamide in diabetic patients and alloxan-diabetic rats. These only served to confirm that in the absence of endogenous or exogenous insulin, even in the smallest quantities, tolbutamide can exert no beneficial action. He is thus forced to the conclusion that the question of how the sulphonylureas act must remain open so long as the mechanism of the action of insulin itself has not been fully explained. He considers that further research into the possibility of the potentiation of exogenous insulin in cases of absolute insulin deficiency is required. *Robert E. Lister*

1023. **The Influence of Salicylate on Hyperglycemia**
S. G. GILGORE. *Diabetes* [*Diabetes*] **9**, 392–393, Sept.–Oct., 1960. 8 refs.

The author has treated 6 diabetic patients at the Jefferson Medical College Hospital, Philadelphia, Pennsylvania, using aspirin as a hypoglycaemic agent [first used in the late nineteenth century]. One patient had been treated previously by diet alone and 2 with insulin. After an initial week on a diet containing 1,800 to 2,000 Calories the patients received aspirin in a dosage of 6 g. daily for 10 days followed by a placebo during a control period of 5 days. The fasting blood sugar level varied from 260 to 504 mg. per 100 ml. before aspirin treatment was started, ranged from 95 to 164 mg. per 100 ml. after 10 days of aspirin administration, and rose to from 185 to 325 mg. per 100 ml. 5 days after treatment ceased. Glycosuria disappeared and the glucose tolerance test gave improved results. Side-effects were mild. The author is investigating this treatment further. [Salicylates and carbohydrate metabolism are discussed fully in an editorial in the same issue of the journal.]
Arnold Pines

1024. **The Frequency of Cancer in Diabetes Mellitus**
G. HERDAN. *British Journal of Cancer* [*Brit. J. Cancer*] **14**, 449–456, Sept. [received Nov.], 1960. 11 refs.

This paper is divided into 6 sections, in the first of which an analysis is presented of the post-mortem records of the Pathology Department of the University of Bristol. The age and sex distribution of the 189 diabetics in this series of 6,317 cases resembled that for diabetes morbidity in the general population. The incidence of malignant tumours among the non-diabetics was 19·5% and that among the diabetics 10·1%, a difference which is shown to be highly significant. In Section 2 a similar analysis is given of data from 7 series of German post-mortem records, in all of which a similar difference of incidence of malignant disease is demonstrated. In Section 3 the validity of various assumptions which may have a bearing on these results is discussed. [A detailed discussion of the variable and influencing factors, distinguishing between those known and those unknown, would have added to the value of this section and helped in the assessment of the final result.]

In Section 4 the incidence of malignant disease and diabetes among in-patients in Bristol Royal Infirmary during the 7 years 1953–9 is studied, the conclusion reached being that these figures seem to support the conclusion drawn from the post-mortem data. In Section 5 a study of sex distribution of the two diseases based on these figures suggests that the negative association is true only for females. In Section 6 the author discusses the findings of other workers on carbohydrate metabolism in diabetes and cancer and the possible influence of diabetes on the incidence of tumours, which differ from the conclusions drawn from the post-mortem data.
Kurt Schwarz

The Rheumatic Diseases

1025. **Clinical Investigation of a New Antirheumatic Combination of Pyrazolone and Pyrazolidine Derivatives.** (Sperimentazione clinica di un nuova anti-reumatico pirazolon-pirazolidinico)
A. Ciocci. *Minerva medica* [*Minerva med. (Torino)*] **51**, 3496–3501, Oct. 17, 1960.

The author of this paper from the Institute of Rheumatology of the University of Rome describes the results obtained in treating 91 patients with "tomanol", a new preparation consisting of 2 parts of "isopyrin" (1-phenyl-2:3-dimethyl-4-*iso*propylamino-5-pyrazolone) combined with one part of phenylbutazone (sodium salt). There were 6 cases of rheumatic fever, 8 of rheumatoid arthritis, 7 of "secondary rheumatism", 38 of osteoarthritis (primary and secondary), 10 of intervertebral disk syndrome, 14 of "arthromyalgic syndromes" of varying aetiology, 3 of trigeminal neuralgia, and 5 of pain due to metastatic tumours.

After routine physical, radiological, and laboratory examination followed by a control period of rest in bed for 5 to 7 days treatment was started with 2 to 4 tablets, 2 suppositories, or 1 to 2 ampoules of tomanol daily [exact dosage not stated] with meals, the dose being increased or diminished subsequently according to effect and tolerance. No other drugs were given, and treatment was continued for at least 3 weeks.

The results of treatment, as judged from the effect on the clinical and humoral signs of rheumatic activity, were "excellent" in 48 cases (53%), "good" in 21 (24%), "fair" in 8 (8%), and "inadequate" in 14 (15%). On the basis of these findings the author considers that tomanol deserves to be added to the list of active antirheumatic drugs. This favourable opinion was confirmed by an additional test on 10 of the patients who had given an excellent or good response to tomanol, but relapsed within one to 4 days when a placebo was substituted. In some cases an ephemeral increase in severity of symptoms was observed after the start of treatment, but this did not prevent a subsequent excellent response. Only 16 patients could be kept under observation, of whom 10 were free of symptoms 40 days after the conclusion of treatment.

Robert E. Lister

1026. **The Use of a New Pyrazolone—Pyrazolidine Preparation in the Treatment of Rheumatic and Traumatic Conditions.** (Considerazioni sull'uso clinico di un nuovo preparato a base di pirazolone-pirazolidina in campo reumatologica e traumatologico)
P. U. Padovani. *Minerva medica* [*Minerva med. (Torino)*] **51**, 3559–3564, Oct. 20, 1960. 20 refs.

Of the various products with an analgesic and antipyretic action "pyramidon" (amidopyrine) and its derivatives are the most effective, but their use is strictly limited by their toxicity and tendency to provoke haematological changes. In this report from the Centro Traumatologico, Bologna, the author describes his experience with "tomanol", a recently introduced compound consisting of 2 parts of 1-phenyl-2:3-dimethyl-4-*iso*propylamino-5-pyrazolone and one of phenylbutazone, in the treatment of 84 patients, of whom 3 were suffering from acute articular rheumatism, 32 from rheumatoid arthritis, 2 from ankylosing spondylitis, 15 from osteoarthritis deformans or "spondylar arthrosis", 10 from periarthritis, epicondylitis, myositis or tendinitis, 10 from various neuritic affections or root pain after intervention for disk hernia, and 12 from osteoarticular and muscular post-traumatic affections. The drug was administered preferably by intramuscular injection, but was also given orally or as a suppository, the dosage varying for each individual case.

Therapeutic effects were rapid and noteworthy in acute and inflammatory cases and in the reactivation phases of chronic cases, but less so in mainly degenerative forms. Post-traumatic and non-articular conditions responded particularly favourably to the treatment. The author found that carefully chosen patients tolerated the remedy well, provided a diet poor in salt was given. He stresses that frequent blood counts should be performed when treatment is protracted, and patients who have suffered previously from gastric or duodenal ulcers must be treated with circumspection; all patients with active ulceration of the gastro-intestinal tract or severe cardio-renal or hepatic insufficiency were excluded from the trial. The over-all therapeutic results were as follows: "very good" 44%, "good" 34·5%, and "fair" 12%, while no benefit was obtained in 9·5%. Side-effects, which occurred in 16·5% of the cases, included nausea, hyperacidity, and vomiting in 7 cases, oedema in 4, and a rash and pruritus in 3. No cardiac or renal complications occurred and no case of agranulocytosis was seen.

Robert E. Lister

ACUTE RHEUMATISM

1027. **Clinical Aspects of Rheumatic Fever in Children.** (О клинке ревматизма у детей)
O. G. Solomatina, G. I. Klajševič, S. M. Levina, and A. A. Ivanova. *Советская Медицина* [*Sovetsk. Med.*] **25**, 3–8, Nov., 1960. 2 figs., 13 refs.

In the authors' experience the clinical picture of rheumatic fever in children has definitely changed in recent years. They base this view on 1,472 cases of the disease in children treated during the period 1953 to 1959, among whom they noted a tendency to an increased incidence among children of pre-school age. Involvement of the joints was much less common in 1959 (12%) than in 1953 (52%) and when it did occur it was mild and of short duration. On the other hand involvement of the vascular system was more frequent, especially in cases with atypical joint lesions such as arthritis of a single

joint or involvement of small joints only. The incidence of endomyocarditis also increased (from 45·4% of 140 cases in 1953 to 73·13% of 186 cases in 1959), while that of pancarditis diminished (from 6·4% of 140 cases in 1953 to only 1·07% of 186 cases in 1959). Clinically, the endomyocarditis developed early (between the 5th and 7th days) and gave rise to murmurs, but not always to permanent valvular damage. At some time during the disease the electrocardiogram showed increased atrioventricular conduction time in 57·0% of cases and prolonged intraventricular conduction time in 77·4%. Persistent increase of the QRS interval was observed in 27% of patients, prolongation of systole in the acute stage in 90% (although this persisted in only 7%), a low-voltage P wave in 82%, and a low-voltage T wave in 93% (the latter recovered slowly in 66%), while other irregularities were seen in a few cases only.

In 1959 also lesions other than cardiac were observed fairly frequently, but their prognostic significance was less serious; lesions of the lung and pleura were rare. Leucocytosis and neutrophilia were more marked in the presence of polyarthritis, polyserositis, and abdominal lesions. In young children the erythrocyte sedimentation rate sometimes remained normal; in 75·5% of these patients the onset was acute, but the course was benign and lasted less than 2 months. Over-all the proportion of acute cases fell from 88·4% in 1953 to 55·3% in 1959, and no fulminant cases were seen in the latter year. Among the other changes seen in 1959 were an increased incidence of mild chorea or chorea associated with cardiovascular involvement and a lower incidence of septic complications. Of the 1,472 young patients treated, 18 aged between 7 and 15 years died. Of these, 2 were admitted to hospital late in the 1st attack with cardiac failure of Grade II or III, but the other deaths occurred in the 3rd to 7th attacks. The immediate cause of death in all cases was pancarditis and circulatory failure. The authors express the view that diagnostic difficulties seem to have increased with the increased incidence of the disease, and to this factor they attribute a recently noted tendency to diagnose rheumatic fever on insufficient grounds. *S. W. Waydenfeld*

1028. **Evolution of Rheumatic Heart Disease in Children: Five-year Report of a Co-operative Clinical Trial of A.C.T.H., Cortisone, and Aspirin**
MEDICAL RESEARCH COUNCIL OF GREAT BRITAIN AND AMERICAN HEART ASSOCIATION. *British Medical Journal* [*Brit. med. J.*] **2**, 1033–1039, Oct. 8, 1960. 11 refs.

A study has been made at the end of 5 years after the conclusion of treatment of the 497 children who were admitted to the U.K./U.S. co-operative clinical trial of the relative merits of A.C.T.H., cortisone, and aspirin in the treatment of acute rheumatic fever [see *Abstr. Wld Med.*, 1955, **18**, 225]. Four hundred and forty-five of the cases (89·5%) were followed for the complete 5 years, and the status of the heart was known for 426 of them. Only 16 (3·2%) had died, 14 of them from rheumatic heart disease; 36 (7·2%) were untraced. The very low fatality rate is striking. At the end of 5 years there is no evidence, on the treatment schedule used in this study, that the prognosis has been influenced more by one treatment than another. This confirms the findings reported at one year.

The major factor in determining the incidence of rheumatic heart disease at the end of 5 years is the status of the heart at the time treatment was begun. For cases without carditis initially the prognosis was excellent, since in 96% there was no residual heart disease. In cases with carditis initially, but without pre-existing heart disease, the proportion without residual heart disease decreased progressively from 82% for those with only a grade-1 apical systolic murmur to 30% for those with failure and/or pericarditis. In cases with pre-existing heart disease the prognosis was poor. Only 30% of those without pericarditis or failure and none of those with pericarditis and/or failure were without heart disease at 5 years. Cases with carditis and without pre-existing heart disease which had recurrences demanding re-treatment during the follow-up period had on the average a more severe cardiac status at start of treatment than did those without recurrences requiring re-treatment. At 5 years a larger proportion of these re-treated cases had murmurs.

These results make it clear that treatment of acute rheumatic fever cannot be properly evaluated unless the status of the heart of the patients at the start of treatment is taken closely into account.—[Authors' summary.]

1029. **Sydenham's Chorea: Its Relationship to Rheumatic Infection and Psychological Illness**
R. MATTHEWS, H. WILLIAMS, W. RICKARDS, I. WATERHOUSE, and J. ALLAN. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 771–774, Nov. 12, 1960. 19 refs.

Twenty consecutive cases of chorea admitted to the Royal Children's Hospital, Melbourne, were investigated by a paediatrician, a psychiatrist, a psychologist, and a social worker in an attempt to determine possible psychological and social aetiological factors. The patients' ages ranged from 4 to 13 years; 7 were boys and 13 girls. Of the 20 patients, 8 had had one or more previous attacks of chorea; 3 gave a history of past rheumatic infection, one of whom had a cardiac murmur; 5 had carditis during the attack of chorea, and one of these had erythema marginatum. In the subsequent 3 years 2 patients had further attacks of carditis and one developed a heart lesion. In 16 cases there was a raised antistreptolysin-O titre and in 10 a raised erythrocyte sedimentation rate. The electroencephalogram (EEG) was abnormal in 16, but there was no correlation between the severity of the chorea (or the side affected in the 6 patients with hemichorea) and the changes in the EEG. Of 13 cases so examined 5 to 18 months after cessation of the chorea, the EEG was normal in 3, less abnormal in 4, unchanged in 5, and worse in one. Psychiatric and psychological data were obtained in 19 of the 20 cases. The average intelligence quotient of the group was significantly below that of the general population, and the group as a whole showed difficulties in educational achievement and school adjustment. Of the 19 patients, 17 showed a common personality pattern, being self-conscious, insecure, overdependent on adults, and afraid

of their own aggressive feelings. Family maladjustment was consistently present. The fathers' occupations varied from unskilled to semi-professional work. Thirteen of the families had suffered financial difficulties in the previous 5 years, and half were in current financial distress. *C. Bruce Perry*

CHRONIC RHEUMATISM

1030. **Polymyalgia Rheumatica: a Clinical Study of 21 Cases**

I. GORDON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 473–488, Oct. [received Dec.], 1960. 4 figs., 15 refs.

In this report from the Aberdeen Royal Infirmary the author describes a series of 21 patients who had a syndrome consisting of pain and stiffness in the muscles and periarticular tissues in relation to the larger joints of the body. There were 11 women and 10 men, and their ages ranged from 49 to 82 years. In 12 in whom the syndrome was fully developed the pain and stiffness were severe enough to immobilize them for a few months. However, joint swelling was observed in only 6 cases; it was transient and affected fingers and knees. There was no radiological evidence of active arthritis. General symptoms were common and consisted of loss of weight, anorexia, fatigue, low fever, and insomnia. The erythrocyte sedimentation rate was raised, ranging from 42 mm. to 122 mm. in one hour (Westergren). There was also hypochromic anaemia, with elevation of the plasma globulin level. The Rose–Waaler test gave a negative reaction in every case.

In 7 cases not treated with steroids the symptoms disappeared completely in 2 to 4 years; in 13 cases there was a prompt remission after steroid therapy was begun. Relapse occurred in 7 cases after the initial course, and two or more courses of steroid therapy were needed.

The author discusses the differential diagnosis from such conditions as cervical spondylosis, secondary carcinoma, myelomatosis, the collagen diseases, and brucellosis. He admits that it may be difficult to distinguish the syndrome from rheumatoid arthritis, but he draws attention to the absence of true arthritis, the absence of joint deformity or ankylosis, and the consistently negative Rose–Waaler reaction. He concludes that polymyalgia rheumatica is a disease *sui generis* which should be treated, when necessary, by short courses of steroids. *K. C. Robinson*

1031. **Intra-articular Nitrogen Mustard Treatment of Rheumatoid Arthritis.** [In English]

K. VAINIO and H. JULKUNEN. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **6**, 25–30, 1960. 1 fig., 10 refs.

The object of the investigation here described was to determine whether, in rheumatoid arthritis, intra-articular injections of nitrogen mustard combined with hydrocortisone gave better results than injections of hydrocortisone alone. The study was carried out, at the Rheumatism Foundation Hospital, Heinola, Finland, on 59 patients with two joints symmetrically involved; where one joint appeared to be more severely involved it was used for the nitrogen mustard injection.

The contents of one ampoule of nitrogen mustard (10 mg.) were diluted to 10 ml. with normal saline; for injection into a knee-joint, for example, 0·5 ml. (0·5 mg.) of the solution was mixed with 25 mg. of hydrocortisone. Injections were given weekly in series of 3 or 6, but in the latter case an interval of 3 weeks was allowed after the first 3 injections. An equal amount of hydrocortisone was injected into the corresponding joint. A number of objective and subjective tests were devised and joints graded both before and after injection. In 32% the combination gave better results than hydrocortisone alone. The best results were obtained in patients with minimal radiological changes—that is, those in whom hydrocortisone alone produced but little effect. *D. Preiskel*

1032. **"Rheumatoid Arthritis" with Negative Serological Reaction**

A. ST. J. DIXON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **19**, 209–228, Sept., 1960. 9 figs., 34 refs.

A follow-up study is reported of 63 cases of rheumatoid arthritis in which the reaction to the sheep-cell agglutination (S.C.A.) test was negative, these representing about 6% of the total number of cases of rheumatic disease admitted to the Manchester Royal Infirmary between 1948 and 1956. A negative reaction is defined as one in which agglutination did not occur with serum dilutions higher than 1:8. Of the 63 patients, 50 were interviewed and examined, 5 were followed up by letter only, 2 were not traced, and 6 had died in the interval. At the follow-up examination it was found that in 12 of the 50 patients the S.C.A. reaction was positive, while in 38 it remained negative. Of the positive reactors, 10 had typical and 2 had atypical rheumatoid arthritis. The course of the arthritis was not different in the 10 reactors from that observed in 24 patients in whom the response to the S.C.A. test remained negative. The author states that the change-over from a negative to a positive reaction may take at least 15 years and possibly longer in some cases. One sero-negative patient with extensive joint involvement and constitutional symptoms died, rheumatoid arthritis being regarded as the cause of death. Another developed myopathy which responded to steroid therapy. Of 9 atypical sero-negative patients, 2 had marked constitutional symptoms, but recovered completely. In one of the patients in this group the disease ran a course suggestive of Reiter's disease to complete recovery and in 2 others the changes were those of mixed osteoarthritis and rheumatoid arthritis. Conditions other than rheumatoid arthritis were present in 11 patients, including psoriasis in 4, gout in one, reticulohistiocytosis in 2, and Takayushu's pulseless disease in one.

The author describes 28 of the cases. He states that the result of the S.C.A. test in general shows a very high degree of positive correlation with clinical signs, a typical clinical picture developing in 10 of the 12 patients who converted from negative to positive. It has been observed that patients making good progress under treatment can become sero-negative, but this does not account

for all the negative results in typical cases of the disease. Some of the atypical cases might be more suitably regarded as examples of other forms of arthritis, such as Reiter's disease, psoriatic arthropathy, and "peri-arthrite rhizomélique". The results of this study confirm the value of a positive reaction to the S.C.A. test which, for purposes of clinical investigation, should now be regarded as an essential feature of rheumatoid arthritis. *William Hughes*

1033. **A Comparison of Prednisolone with Aspirin or Other Analgesics in the Treatment of Rheumatoid Arthritis**
A Second Report by the Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, ACTH, and other Therapeutic Measures in Chronic Rheumatic Diseases. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **19**, 331–337, Dec., 1960. 1 ref.

A previous report (*Ann. rheum. Dis.*, 1959, **18**, 173; *Abstr. Wld Med.*, 1960, **27**, 399) described the results obtained in the first 2 years of a controlled comparison between prednisolone and aspirin or other analgesics in the treatment of rheumatoid arthritis. The present report deals with developments during the third year of the trial. The total number of patients in the trial at the end of the second year was 76, of whom 35 had been given analgesics only and 41 had been given prednisolone only. During the third year 9 of the former group received prednisolone in addition to analgesics and 7 of the latter group were no longer given prednisolone, one receiving dexamethasone, one cortisone, one aspirin, and 4 no drugs at all. The mean daily dose of prednisolone rose from 10 to 10·5 mg.

There was little change in the general situation as between the two main groups during the third year, though many patients in both groups deteriorated slightly and one or two improved. Assessment of the clinical condition of the patients with reference to grade of disease activity, functional capacity, degree of joint pain and swelling, strength of grip, and erythrocyte sedimentation rate showed that the advantage to prednisolone demonstrated previously was still present after 3 years to a significant, though slightly lower, degree. The radiological appearances deteriorated a little in both treatment groups, and the initial advantage to the prednisolone group in this respect may have been caused by a higher dosage level in the first year. The initial tendency for sheep-cell agglutinating titres to rise in the prednisolone group did not continue and there was some reduction in the number of patients with very high titres. No major complications of prednisolone treatment were observed in the third year. *J. A. Cosh*

1034. **An Association between Ulcerative Colitis, Regional Enteritis, and Ankylosing Spondylitis**
E. D. Acheson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 489–499, Oct. [received Dec.], 1960. 29 refs.

During an epidemiological study of ulcerative colitis and regional enteritis in United States veterans a surprising number of patients were found to have ankylosing spondylitis in addition. Data were obtained from all 2,320 patients discharged from Veterans Administration Hospitals with regional enteritis between 1953 and 1957 and ulcerative colitis in 1956 and 1957. It was found that 31 of the cases of colitis (representing 2·6% of discharges) and 22 of the cases of enteritis (representing 3% of discharges) had spondylitis. This diagnosis of spondylitis was made 20 times as often as in a 25% systematic sample of all patients admitted to Veterans Administration hospitals. Information was also collected regarding two other chronic diseases; thus among 675 admissions for Hodgkin's disease no cases of spondylitis were found, and in 813 cases of disseminated sclerosis there were only 2 of spondylitis.

The author gives in detail the diagnostic criteria for the conditions under discussion. He notes that 24 patients with spondylitis showed the classic picture of the advanced stage of the disorder, with obliteration of the sacro-iliac joints and extensive ankylosis of the spine. In the majority of cases the spondylitis preceded the abdominal condition. Deep irradiation had been given in 14 cases, but in 8 this was after the onset of the enteritis or colitis; in only 6 cases out of the total could irradiation have played any part in the development of these conditions. *K. C. Robinson*

SYSTEMIC LUPUS ERYTHEMATOSUS

1035. **Further Observations on Hepatitis and Cirrhosis in Young Women with Positive Clot Tests for Lupus Erythematosus**
L. G. Bartholomew, J. C. Cain, A. H. Baggenstoss, and A. B. Hagedorn. *Gastroenterology* [*Gastroenterology*] **39**, 730–736, Dec., 1960. 7 refs.

Three additional cases of an unusual disease of the liver occurring in young women with a positive lupus erythematosus clot test are reported. This disease is characterized by a distinct clinical syndrome which includes many of the following features: periodic fever, migratory polyarthritis, pleurisy, indeterminate abdominal pain, unusual sensitivity to sunlight and drugs, skin rashes, weakness, and fatigue. Later in the course of the disease, evidence of serious impairment of the liver, including jaundice, hepatosplenomegaly, and spider angiomas, overshadows some of the former systemic manifestations.

Typical laboratory findings in the fully developed syndrome include anemia, frequently hemolytic in type; leukopenia; marked elevation of the sedimentation rate; marked hypergammaglobulinemia; varying degrees of jaundice; significant abnormalities in the so-called liver function tests, including the cephalin flocculation and thymol and zinc turbidity tests; fixed elevation of the prothrombin time; false positive serologic reaction for syphilis; and abnormal urinary sediment. The clot test for lupus erythematosus has given repeatedly positive results.

Despite these clinical and laboratory abnormalities and the ultimate poor prognosis, patients present for a considerable time the appearance of good health, belying the seriousness of their illness. Death is due to hepatic insufficiency.—[Authors' summary.]

1036. **Systemic Lupus Erythematosus. Description of 37 Cases in Children and a Discussion of Endocrine Therapy in 32 of the Cases**

C. D. Cook, R. J. P. Wedgwood, J. M. Craig, J. R. Hartmann, and C. A. Janeway. *Pediatrics* [*Pediatrics*] 26, 570–585, Oct., 1960. 10 figs., 11 refs.

The authors have reviewed 37 cases of systemic lupus erythematosus in patients aged under 14 seen between 1916 and 1959 at the Boston Children's Hospital and the Babies and Children's Hospital, Cleveland. Of these children, 34 were girls. In 30 cases the illness started between the ages of 9 and 13, and 27 of the children died within 8 weeks to 5¼ years of the onset. In 7 cases severe sore throat and in 4 considerable psychological stress preceded the illness.

A facial rash was present at some stage of the disease in 31 cases; 19 patients presented with an erythematous rash, which was accompanied by fever and arthralgia in 15 cases. In 12 cases there was intermittent arthralgia, sometimes with fever, for up to 3 years before the facial rash. In 4 children thrombocytopenia, in 5 renal manifestations, and in 2 cardiac failure were early features. Fulminating illness with death in 2 to 6 months occurred in 5 cases. The facial rash did not show the involvement of the upper eyelid and the oedema that are seen in dermatomyositis. In the later stages vesicular, bullous necrotic, or haemorrhagic lesions sometimes developed; rashes resembling measles, drug eruption, and herpes zoster also occurred. Half the children developed erythematous macules on the hands and feet which were sometimes intensely pruritic. Some children had finger nail-bed changes. A quarter of the patients had partial alopecia. Oral and genital lesions were also observed. All but 4 patients showed renal involvement characterized by oedema and hypertension, which was an important factor in the death of 18. Hepatomegaly was noted in 15 cases and significant splenomegaly in 16. Generalized lymphadenopathy was not prominent. Pericarditis occurred in 3 cases without uraemia. Pleural effusions and pneumonia were common, and cardiac abnormalities were noted in 20 cases. One-third of the patients had neurological symptoms, including convulsions, hemiplegia, and muscle weakness. In one case cytoid bodies were found in the fundus oculi.

Before antibiotics were available infections were troublesome and caused 3 deaths. In 6 cases there was difficulty in cross-matching blood, and some of these patients gave a severe reaction to transfusion of most carefully cross-matched blood.

The L.E. test gave positive findings in 31 of the 32 patients tested. Normochromic normocytic anaemia was common, and 20% of the children developed an anaemia with a haemoglobin level below 6 g. per 100 ml. Leucopenia with a cell count below 5,000 per c.mm. occurred in 21 cases, and the leucocyte response to infection was often decreased. Six patients had a biologically false positive reaction for syphilis. The latex fixation test gave a negative response in the 8 cases tested. Reticulocytosis up to 10% occurred following a favourable response to cortisone. Positive results were obtained in 20 of 22 children on whom liver flocculation tests were performed. The injection of leucocytes intradermally led to a delayed hypersensitivity reaction with redness and oedema within 48 hours.

All the 14 cases examined post mortem showed involvement of the glomeruli or arterioles of the kidney. Libman–Sacks lesions occurred in 7 cases. In 10 cases plasma-cell hyperplasia was found in the spleen, bone marrow, or lymph nodes. Vascular involvement led to gastro-intestinal ulceration and infarction of the liver, spleen, and pancreas. Haematoxylin bodies were seen in most cases.

Treatment included gold therapy, administration of bismuth and of nitrogen mustard, and irradiation. Of 3 children given nitrogen mustard, partial remission occurred in 2. Cortisone was used in 32 cases. Because attempts to reduce the dose usually led to relapse, continuous treatment with high doses was employed. In 6 of the 10 surviving patients cortisone treatment reversed abnormal urinary findings. Such reversal had not been observed by the authors in inadequately treated cases, but some renal lesions progressed in spite of steroid therapy.

The authors conclude that systemic lupus erythematosus is more severe in children than in adults. Because of the poor prognosis of the disease and the evidence suggesting the value of steroid therapy, they advocate early and continuous treatment with high doses of steroids for several years even in the absence of symptoms.

G. L. Asherson

1037. **Demonstration of L.E. Cells at Local Inflammatory Sites in Patients with Systemic Lupus Erythematosus**

P. E. Périllie, P. Calabresi, and S. C. Finch. *New England Journal of Medicine* [*New Engl. J. Med.*] 263, 1052–1055, Nov. 24, 1960. 4 figs., 14 refs.

In this study of the L.E.-cell phenomenon, reported from Yale University School of Medicine, New Haven, Connecticut, the authors applied cover-slips to the abraded skin of 11 patients with systemic lupus erythematosus to observe the development of L.E. cells *in situ*. In 5 of the 11 cases L.E. cells were found adhering to the cover-slips removed 2 to 7 hours after application. Serial examinations showed all stages of L.E.-cell development. The 6 cases in which a negative result was obtained had received corticosteroid therapy for at least 2 weeks before the test, and it is suggested that the failure to detect L.E. cells in these cases may be due to the decrease in L.E. globulin which is known to occur after such treatment. No L.E. cells were found on cover-slips taken from 36 control subjects who were not suffering from systemic lupus erythematosus. The authors conclude that the cover-slip method is " probably as sensitive as most L.E.-cell tests now in use and may serve as an additional simple diagnostic aid in systemic lupus erythematosus ".

M. Wilkinson

1038. **Avascular (Aseptic) Bone Necrosis Associated with Systemic Lupus Erythematosus**

E. L. Dubois and L. Cozen. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 174, 966–971, Oct. 22, 1960. 4 figs., 10 refs.

Physical Medicine

1039. A Study to Determine the "Energizing" Effects of Iproniazid (Marsilid) on a Group of Hemiplegics

C. CASELLA and J. SOKOLOW. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **41**, 381–385, Sept., 1960. 20 refs.

An attempt to stimulate hemiplegic patients to take a more enthusiastic part in measures for their rehabilitation is described in this paper from Elmhurst General Hospital, New York City. It is pointed out that for a variety of reasons many such patients lack "motivation" to try to recover. Since some workers have found that iproniazid has "energizing" properties this drug was given to 30 such patients for a period of 6 weeks, while 30 received a placebo, the double-blind technique being employed. At the end of 6 weeks there was a statistically significant improvement in physical activity of the treated group compared with the untreated, but analysis of the scores in the Rorschach test showed no significant difference between the two groups. Possible causes of this discrepancy are discussed, one suggestion being that iproniazid energizes at the physical level, but does not affect the personality. *W. Tegner*

1040. Correlation between Fibrillation Potentials and Abnormal Chronaxies

W. T. LIBERSON and R. PAVASARS. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **41**, 346–350, Aug., 1960. 2 figs., 10 refs.

The authors describe an electromyographic study carried out at various Veterans Administration Hospitals on 101 patients with peripheral neuropathy, nerve injury, myelopathy, or myopathy, a total of 1,620 muscles being examined. Muscle chronaxie was measured by means of a constant-current chronaximeter and muscle potentials with a coaxial needle connected to a recording electromyograph. Chronaxies of over one millisecond were considered abnormal, except in the hamstrings and the extensor hallucis longus, for which 3 msec. was the limit. Fibrillation potentials are defined as spontaneous spikes with a duration of less than 2 msec. occurring in resting muscle.

In patients with a diffuse neuropathy a chronaxie over 20 msec. is associated with fibrillation; if the chronaxie is between 10 and 20 msec., 60% of the muscles fibrillate, if between 3 and 9 msec. 30% of muscles fibrillate, and only 20% of muscles with a slight increase of chronaxie fibrillate. In these patients 13% of muscles with a normal chronaxie showed fibrillation. In patients with nerve injuries fibrillation occurred in nearly all cases if the chronaxie was over 3 msec., and about 30% of the remainder had fibrillation. Lesions of the anterior horn cells were associated with fibrillation in 50% of muscles if the chronaxie was over 10 msec. and in 25% of muscles with a chronaxie below 3 msec. Myopathic patients all had chronaxies below 10 msec. and fibrillation was found in half the muscles with a chronaxie of 3 to 10 msec. and in 20% of the remainder. Consequently an abnormal chronaxie is not always associated with fibrillation as revealed by this technique, and therefore the performance of both tests is advocated. The authors also discuss strength–duration curves and show that these may give a false picture of normality when partial denervation is present, but that measurement of chronaxie may be diagnostic. *J. B. Millard*

1041. The Physiotherapy of Headache of Cervical Origin. (Les céphalées d'origine cervicale. Leur traitement physique)

L. ISÉMEIN and L. PERDRIX. *Annales de Médecine physique* [*Ann. Méd. phys.*] **3**, 13–16, Jan.–Feb. [received Dec.], 1960.

As the neck is daily exposed to the risk of trauma rheumatologists often see cases of headache of cervical origin; in women this is sometimes associated with endocrine disturbance, for example at the menopause. Soft tissues are frequently involved and radiography cannot replace a careful clinical examination. The authors are not here concerned with headache due to general medical causes, to osteitis, to neoplastic metastases, or to true migraine, but they point out that migraine-like headache may arise from a source of irritation in the cervical spine. The symptoms of this include cranial paraesthesia, a sensation of "water running down the skin", itching, tinnitus, retro-orbital or retro-ocular pains, pain in the face, and vertigo without actual loss of equilibrium. They may be brought on by prolonged fixation of the neck in one position or by sudden change of position. Physical examination must include deep and systematic palpation of the neck, which frequently reveals the presence of fibrositic nodules which feel like "grains of sand" in the muscles. There may be tenderness at the point of insertion of tendons in the region of the spinous or transverse processes. Muscular spasm and vertebral displacements or subluxations may also be detected. Radiographic films should include antero-posterior, lateral, and oblique views, but the presence of arthrosis in a patient aged 50 or over does not necessarily establish the cause of the headache.

In regard to treatment, fibrositis yields to deep, though admittedly painful, massage carried out every 4 to 8 days, and myositis requires somewhat similar treatment. The presence of muscular spasm, which must be treated energetically, contraindicates the use of traction or manipulation, but the application of heat or cold and massage, as well as administration of analgesics and sedatives, are all useful. Traction gives good results in cervical-disk lesions and subluxations, but must be used with care. In resistant cases radiotherapy with doses of the order of 100 r. may be considered. Finally, it is stressed that many of these patients are frail, that their reactions to treatment vary greatly, and that they must be handled with caution.

[Some of the views expressed in this paper will be unacceptable to British clinicians, and treatment by immobilization by means of a collar is not even mentioned.]

D. Preiskel

1042. **Effect of Short Bouts of Isometric and Isotonic Contractions on Muscular Strength and Endurance**

C. E. WALTERS, C. L. STEWART, and J. F. LECLAIRE. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **39**, 131–141, Aug. [received Oct.], 1960. 6 figs., 22 refs.

The published results of investigations into the relative efficacy of isometric and isotonic methods of exercise in the production of increased strength, increased endurance, and retention of the improvement of strength are somewhat conflicting. In the investigation herein reported 15 young adults specializing in physical education at the Florida State University, Tallahassee, underwent a series of trials in an attempt to compare these different methods of developing elbow flexor strength. One group trained by exerting the full isometric strength, a second exerted two-thirds of the full isometric strength, and a third practised isotonic contractions at one-third maximum strength as rapidly as possible. Training in this way was confined to three 15-second periods daily for 8 days. Strength and endurance were measured before and after training in both preferred and non-preferred arms, and at 3 and 8 weeks after training.

Because of the small number of subjects, significant results were not always obtained. Full isometric contraction was more effective than isometric contraction at two-thirds full strength and was about as good as isotonic training. Endurance, as measured by the maximum number of isotonic repetitions possible, was improved in all groups, but most markedly in the full isometric group. The improvement shown was not only retained when retested at 3 and 8 weeks after training, but had usually increased further. Consistent increases in strength in the non-preferred arm were also shown. It also appeared that improvement as measured by one method of testing was not dependent upon the same method of training being employed. *B. E. W. Mace*

1043. **Effect of Sauna Bath on Fibrinolysis**

M. MIETTINEN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **15**, 943–944, Sept. [received Nov.], 1960. 1 fig., 10 refs.

The effect of sauna baths on the fibrinolytic activity of the blood plasma was studied at the Institute of Occupational Health, Helsinki. A sauna bath, which is taken weekly by a large part of the population of Finland, is a steam bath consisting in washing with soap and water and successive exposures to hot humid air and cold water. Of 24 healthy policemen and firemen, aged 24 to 53, 12 took a sauna bath on one occasion and 12 served as controls; 2 to 4 weeks later the groups were reversed. A sample of blood was taken before and then immediately after the bath, a third sample 2 hours later, and a fourth next morning—that is, 12 hours after the bath. Fibrinolysis was determined by the method of Fearnley and Lackner (*Brit. J. Haemat.*, 1955, **1**, 189). From the cubital vein 8 ml. of blood was taken by means of a large-bore needle connected with a plastic tube leading to a sterile siliconized centrifuge tube in an ice bath. After centrifugation at 4° C. 0·2 ml. of plasma was transferred to a glass tube containing 1·8 ml. of a buffer solution. The tubes were placed in an incubator at 37° C. and inspected every hour for 24 hours, then 2-hourly until the fibrin clot had disappeared.

The fibrinolysis time of the sample taken immediately after the bath was found to be significantly decreased. No difference was observed between the test and control groups in the fibrinolysis time of blood taken 2 hours or later after the bath.

The author points out that an increase in fibrinolytic activity of plasma has been reported in several kinds of stress situations, including exercise, acute emotional stress, and surgical operation. *Kenneth Stone*

1044. **Treatment of Osteoarthritis of the Hip by Mobilization under General Anaesthesia followed by Functional Re-education.** (Traitement de la coxarthrose par mobilisation sous anesthésie générale suivie de rééducation fonctionnelle)

S. DE SÈZE and A. DENIS. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **27**, 182–185, June, 1960. 1 fig.

The treatment of 15 patients with osteoarthritis of the hip by the method of Staudinger, which consists in manipulation under general anaesthesia followed by graduated intensive physical treatment, is described. In carrying out the procedure the hip-joint of the anaesthetized patient is slowly flexed in adduction to the maximum extent, this movement being followed by rotation and then by abduction of the extended leg. After the manipulation the legs are immobilized in abduction for 36 hours, during which time analgesics are necessary. Thereafter the patient is shown how to perform static contractions of the muscles of the trunk and thighs; on the third day he sits over the edge of the bed, while on the fourth he may walk a few paces with the help of an appliance. At this stage correction of the gait is important; walking distance may then be gradually increased. After about 2 weeks the patient is ready for transfer to a rehabilitation centre for further intensive treatment. Non-manual occupations can usually be resumed during the third month after manipulation. Of the 15 patients so treated, 5 achieved appreciable increase in range of movement and disappearance of pain, 6 showed partial amelioration, but 4 were not benefited. It is noted that the presence of osteoporosis or a past history of phlebitis or other vascular disorder is a contraindication to this form of treatment.

In the authors' opinion this treatment is of most benefit on the one hand to the patient aged about 50 with unilateral and early osteoarthritis of the hip and on the other to the older patient with bilateral disabling arthritis of the hips who is too old for surgical treatment but is otherwise healthy; in such cases the deformity can be corrected and pain is often much relieved. Further work is needed, however, to assess more accurately the value of the method. *B. E. W. Mace*

Neurology and Neurosurgery

1045. **Sensitivity to Pain in the Aged**
E. D. SHERMAN and E. ROBILLARD. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 944–947, Oct. 29, 1960. 20 refs.

At the Montreal Hebrew Old People's Home and the University of Montreal the authors have investigated the assertion that perception of pain is reduced in old age. The 200 subjects studied were drawn from the three ethnic groups making up the population of Montreal—Anglo-Saxon, French, and Jewish. They were divided into two main groups, 110 men and women aged 65 to 97 and 90 men and women aged 20 to 30 years. Sensitivity to pain was determined by measuring the pain-perception threshold (subjective) and the pain-reaction threshold (first objective evidence of withdrawal from the stimulus). The stimuli for cutaneous pain were provided by varying intensities of light focused on the forehead of the subject by the Hardy–Wolff–Goodell dolorimeter. To prevent reflection, to minimize penetration of visible light into the skin, and to convert radiant into molecular energy, in which form heat is conducted through the epidermis to the pain endings, the subject's forehead was blackened with indian ink. Each test consisted of 10 to 14 exposures with a 2-minute interval between each.

A significant elevation of both thresholds with age was constantly noted in all groups. The threshold values for males of all ages tended to be higher than those for women. The mean responses of the French and Jewish groups were of the same magnitude, but the average response of the Anglo-Saxon group was significantly higher than that of the combined French and Jewish groups, though no definite conclusion could be drawn from these findings. *A. C. F. Green*

1046. **Fallacies in Interpretation of Queckenstedt's Test**
A. R. TAYLOR. *Lancet* [*Lancet*] **2**, 1001–1004, Nov. 5, 1960. 6 figs., 23 refs.

The author first rapidly reviews the various interpretations and misinterpretations that have been made of the test introduced in 1916 by Queckenstedt, who showed that compression of the jugular veins caused an increase of pressure in the cerebrospinal fluid (C.S.F.), but that in the presence of a lesion blocking the subarachnoid space this increase was not transmitted to the spinal canal.

He then describes, from the Royal Victoria Hospital, Belfast, 7 cases of neurinoma or meningioma occurring between C1 and C4 in which apparently complete subarachnoid obstruction was demonstrated by myelography or at operation, although Queckenstedt's test had previously given a negative result. It therefore seemed likely that the obstruction was being by-passed by transmission of the increased venous pressure through the vertebral plexuses: venous dye-injection studies (fully described) performed on the cadaver and in monkeys provided confirmatory evidence of this hypothesis. The author stresses the importance of venous distension as the primary cause of the rise in C.S.F. pressure in Queckenstedt's test and points out that it is not due to increased formation of C.S.F. in the ventricles, as postulated by Dandy and Blackfan. In conclusion he shows that Queckenstedt's test is not reliable as a test of cervical spinal obstruction above the level of C5–6 unless both the extradural and intradural vertebral veins are also completely obstructed by the agent compressing the spinal cord. *I. Ansell*

1047. **The Electroencephalogram in Acute and Chronic Cerebrovascular Disease.** (Das EEG bei akuten und chronischen zerebrovaskulären Erkrankungen)
C. SPUNDA. *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* [*Wien. Z. Nervenheilk.*] **18**, 73–94, 1960. 41 refs.

At the Rosenhügel Neurological Hospital, Vienna, the author has analysed the electroencephalograms (EEGs) of 958 patients with various types of acute and chronic cerebrovascular illness which were diagnostically grouped as follows: (1) intracerebral haemorrhage; (2) transient cerebrovascular incidents; and (3) chronic cerebrovascular processes. The over-all incidence of EEG abnormalities of all types for the entire series was 78·7%, being 83% each in Groups 1 and 2 respectively, and 69% in Group 3. An abnormal EEG was most often found within 3 days of the incident or in patients with disturbed consciousness. Patients with only transient lesions or lesions in the cerebellum–brain-stem area and those with chronic processes with few clinical signs showed a high percentage of normal or borderline EEGs. *J. Hoenig*

1048. **The Pathogenesis and Management of Spinal Myelomeningocele**
E. D. SMITH. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 801–804, Nov. 19, 1960. 2 refs.

The author discusses the natural history, pathology, and treatment of spina bifida cystica as seen in 214 children at the Royal Children's Hospital, Melbourne, during the 15 years ending June, 1958, of whom 183 had myelomeningocele and 31 simple meningocele. Of the 183 infants with myelomeningocele, 119 (68%) have died, and of the 56 (32%) still alive, the degree of locomotor disability is major in 29 and minor in 18 (there being none in 9 cases), while only one patient has normal urinary control and only 4 have bowel control. Hydrocephalus had been present in 25 of the survivors. Of the infants with myelomeningocele, 50% died in the first 6 weeks of life and most of the others during the first year, deaths in this period being mainly due to progressive hydrocephalus with or without meningitis; after the first year bladder complications accounted for the

majority of the deaths. In this series the over-all risk of meningitis in ulcerated myelomeningocele was 35% and parenteral antibiotics were found to be of little value prophylactically. Apart from being a cause of death meningitis may cause ascending myelitis, thrombophlebitis, and subarachnoid adhesions, which tend to increase the degree of hydrocephalus. Operation shortly after birth, however, was of prophylactic value. Of 33 cases with incomplete skin cover operated on in the first month, only 3 developed meningitis. The author suggests that all patients with myelomeningocele have, or have had, some degree of hydrocephalus. Some may have compensated *in utero* or in early post-natal life, but definite evidence of hydrocephalus was found in 77% of the present cases. Of the patients in whom the hydrocephalus was not treated, only one in 5 survived. It has been shown that in 90% of such hydrocephalic children the hydrocephalus is either present at birth or reveals itself within 5 to 6 weeks; it very rarely appears after the 8th week.

The aetiology of myelomeningocele is unknown. Inquiry revealed no evidence of any abnormal exogenous influence during pregnancy in this series, but a sibling in the same family was found to be affected in 7·8% of cases, while another congenital abnormality in other siblings was found in a further 2·4%. Discussing these findings and the prospects and consequences of early and late operation, the author suggests that, unless frank rupture with deflation of the sac requires early closure and except where minimal neurological defects are present and simple closure possible, surgery should be delayed for 5 to 6 weeks. By then a full assessment of the situation is possible and also the infant's back will possibly have healed somewhat. Thereafter a full programme can be planned, a decision taken as to whether the hydrocephalus requires priority operation or not, and how orthopaedic and other treatment may best be carried out. *Janet Q. Ballantine*

BRAIN AND MENINGES

1049. **Benign Intracranial Hypertension Due to Adrenal Steroid Therapy**

P. F. Benson and P. O. D. Pharoah. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **109**, 212–218, 1960. 40 refs.

The authors use the term benign intracranial hypertension for those cases in which considerable increase in the intracranial pressure is not due to any focal neurological lesion and describe 2 cases seen respectively at Guy's Hospital and Evelina Children's Hospital, London. The first patient, an 8-year-old boy with eczema, had received 10 mg. of prednisolone daily for a year. The dose was reduced to 5 mg. daily and a week later signs of intracranial hypertension developed—headache, vomiting, drowsiness, and papilloedema. These signs disappeared in 2 months after prednisolone was withdrawn. The second patient, a boy of 5½ years, also had eczema and had been treated for 16 months by local application of 1% hydrocortisone ointment. Similar symptoms developed and cleared up quickly when the hydrocortisone ointment was discontinued. The fundi were normal in 4 weeks. The authors consider that the symptoms were due to administration of the steroid and not, as was possible in the first patient, to withdrawal of the steroid. *M. C. G. Israëls*

1050. **Diseases of the Basal Ganglia: Their Relation to Disorders of Movement.** [The Croonian Lectures]

D. Denny-Brown. *Lancet* [*Lancet*] **2**, 1099–1105, Nov. 19, 1960, and 1155–1162, Nov. 26, 1960. 14 figs., bibliography.

1051. **Aneurysms Arising from the Point of Origin of the Vertebral Artery**

D. K. Spindle and K. H. Abbott. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **25**, 130–139, Sept. [received Nov.], 1960. 4 figs., 19 refs.

The authors report 12 cases of aneurysm of the vertebral artery; only 2 [it is not clear which] were seen before death, the others being collected from the necropsy files of the Los Angeles County Hospital. They discuss the clinical features of these cases in the light of 100 cases reported in the literature. They consider that vertebral aneurysms can best be classified into 3 clinicopathological groups: (1) large saccular aneurysms giving signs and symptoms relative to their mass and thus appearing not unlike posterior-fossa tumours; (2) berry aneurysms, which manifest themselves by subarachnoid bleeding; and (3) those found incidentally at necropsy. Diagnosis, however, presents some difficulty. The large aneurysms usually present with episodic nuchal or suboccipital pain, often exacerbated by change of posture; vertigo, nausea, unilateral cerebellar signs, and cranial palsies also occur, and often the picture suggests a lesion of the cerebello-pontine angle. Bilateral motor signs have been reported in " a fair number " of cases. Of the 5 cases in the present series in which the aneurysm bled, loss of motor power occurred as an initial symptom in 3 cases—described as " my legs and arms went dead ", " I crumpled to the floor powerless "—otherwise the symptoms were those of a typical subarachnoid haemorrhage. It is emphasized that vertebral angiography must be performed on both sides if these aneurysms are not to be missed. *N. S. Alcock*

1052. **Vertebral Artery Compression in Cervical Spondylosis: Arteriographic Demonstration during Life of Vertebral Artery Insufficiency Due to Rotation and Extension of the Neck**

S. Sheehan, R. B. Bauer, and J. S. Meyer. *Neurology* [*Neurology* (*Minneap.*)] **10**, 968–986, Nov., 1960. 11 figs., bibliography.

From Wayne State University College of Medicine, Detroit, the authors report in considerable detail the clinical and arteriographic findings in 26 out of 46 patients who were suffering from what they consider to be a well-defined disease entity for which they propose the name " spondylotic vertebral artery compression ". Defects in the vertebral arterial blood flow were demon-

strated by a simple percutaneous method (fully described) of performing transbrachial vertebral arteriography, the catheter inserted in the brachial artery being passed up to the subclavian artery near the origin of the vertebral artery. The vertebral and basilar arteries are then visualized in two planes and in several positions of the head while seven injections of diatrizoate to a total volume of 130 ml. are given. The carotid arteries may also be visualized by a further injection of 40 ml. of the medium. Only 4 minor, transient, complications occurred during these exhaustive investigations.

In the 26 patients, 18 men and 8 women ranging in age from 43 to 74 years, the most common symptom was dizziness and/or vertigo, other frequent signs or symptoms being blurred vision, headache, and peculiar attacks of collapse (" drop attacks ") which occurred suddenly without loss of consciousness. Signs of nerve-root compression were not necessarily present, although they frequently were. Other disturbances due to vertebral arterial compression included spasticity, ataxia, nystagmus, visual field defects, ophthalmoplegia, and motor cranial nerve weakness. A most significant, indeed pathognomonic, sign was that symptoms such as blurred vision, nystagmus, and dizziness could be produced at will by rotating and hyperextending the head. Cervical spondylosis was demonstrated in all cases in the plain x-ray films, while angiography showed that the vertebral arteries were distorted or compressed and that the distortion was accentuated by rotation of the head. Atherosclerotic lesions appeared to co-exist fairly frequently in the parts of the vessel subjected to compression.

Full case reports are presented and the arteriographic findings are illustrated. The possibility of treatment with anticoagulant drugs is discussed and it is considered that good results may be obtained thereby.

J. B. Cavanagh

1053. **Soviet Investigations in the Field of the Vascular Supply of the Brain.** [Review Article]
N. I. GRASHCHENKOV, B. N. KLOSOVSKII, E. N. KOSMARSKAIA, and L. N. SISKIN. *Archives of Internal Medicine* [*Arch. intern. Med. (Chicago)*] **106**, 532–570, Oct., 1960. 30 figs., bibliography.

1054. **Phantom Orgasm in the Dreams of Paraplegic Men and Women**
J. MONEY. *Archives of General Psychiatry* [*Arch. gen. Psychiat.*] **3**, 373–382, Oct., 1960. 12 refs.

The author reports from Johns Hopkins Hospital, Baltimore, that in interviews of at least one hour's duration an attempt was made to elicit data on the cognitional eroticism and dream eroticism of 14 men and 7 women suffering from complete paraplegia or quadriplegia; no cases of incomplete spinal interruption were included in the study. None of the patients were too inhibited to talk frankly about sex. A likely relationship between old age and lack of sexual imagery in dreams was found, since the 2 women and one man in the series over the age of 60 reported none. Also it appeared that the longer the interval between the injury and the date of the interview, the less the imagery. The content of sexual imagery in dreams did not change significantly from what it had been before injury and there was no evidence either that it changed in type after injury. However, orgasm imagery in dreams was not predictable on the basis of its frequency in dreams before injury.

The author concludes that for these patients sex is a matter of memory and is not striven for as in those still receiving sensation from the genito-pelvic area. He points out that this is a significant finding since it offers conclusive evidence that the brain can generate erotic experience independently of the genitalia, just as in paraplegics the genitalia can work reflexly without connexion with the brain. The imagery of orgasm in sleep dreams may thus be considered as a special example of the phantom phenomenon, since the sensation or imagery could not be attributed to stimuli from the genitalia.

G. de M. Rudolf

1055. **Cerebrovascular Accidents in Patients Receiving Anticoagulant Drugs**
C. E. WELLS and D. URREA. *Archives of Neurology* [*Arch. Neurol.*] **3**, 553–558, Nov., 1960. 28 refs.

Experiments in dogs have suggested that administration of anticoagulant drugs before or immediately after induction of cerebral embolism results in an increase in the area of haemorrhagic infarction with a consequent increase in mortality. However, a review of reported cases of cerebrovascular accidents during anticoagulant therapy does not permit any definite conclusions to be drawn on the untoward effects of such treatment in man.

Of over 600 patients receiving long-term anticoagulant therapy for various conditions at the Anticoagulant Clinic, New York Hospital, 23 had a total of 26 cerebral accidents during treatment: intracranial haemorrhages (5 of which were subdural) in 14 instances, cerebral emboli in 9, and cerebral thromboses in 3. Of these 26 episodes, 7 occurred when the prothrombin time was above the therapeutic range and 6 when it was below that range. There were 9 deaths in the series; 8 were due to haemorrhage and one was the result of embolism. Of the 9 deaths, 6 occurred in hypertensive patients, 5 of whom had had intracranial haemorrhage. In the authors' view the danger of cerebral vascular accident appears greater in hypertensive than in normotensive patients. Further, the high incidence of subdural haematomata indicates that relatively slight head trauma may lead to this complication when anticoagulants are administered.

R. Wyburn-Mason

1056. **Traumatic Epilepsy after Closed Head Injuries**
W. B. JENNETT and W. LEWIN. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 295–301, Nov., 1960. 14 refs.

After indicating the manner in which selection of cases may affect the apparent incidence of epilepsy after head injury the authors describe their observations on 1,000 consecutive cases of closed head injury admitted to the Radcliffe Infirmary, Oxford. Excluded from the analysis were 179 cases occurring in patients who had been transferred from other hospitals as needing special care. The onset of epilepsy was divided into early (usually within one week of injury) and late (mostly after 3 months

from the time of injury). The incidence of early epilepsy in this series was 3·9%, and late epilepsy appeared in 7·5% of cases without early epilepsy and in 28·5% with early epilepsy. However, early and late fits after trivial injuries were confined to children, and no adult with a mild injury with less than 24 hours' post-traumatic amnesia and without depressed fracture of the skull or intracranial haemorrhage developed late epilepsy, even if there had been early fits. Post-traumatic amnesia of more than 24 hours' duration, depressed fracture of the skull, and intracranial haematoma were all factors which increased the frequency of early epilepsy; but early fits without other signs of cerebral compression were never the only sign of an intracranial haematoma. When the influence of prolonged post-traumatic amnesia, depressed fracture, and intracranial haematoma was considered in the cases of late epilepsy it was found that intracranial haematoma was the only single factor which produced a greater incidence of late epilepsy than the group as a whole (nearly one-third). Prolonged post-traumatic amnesia and depressed fracture occurring together produced the highest rate of late epilepsy in all groups studied (46·6%), although neither alone carried a serious risk of epilepsy. This high incidence due to the two factors combined approaches that of epilepsy after penetrating missile wounds (nearly 50%). In this series all but one case of early epilepsy developed during the first week, and there was then a period of some 3 months before late epilepsy began to develop. Of the patients with late epilepsy, 50% had had their first fit by the end of the first year and 70% by the end of the second year. A further, more detailed, study of late epilepsy is promised by the authors. *J. B. Stanton*

1057. Relationship between Candidacy and Outcome in Surgery for Parkinsonism

TUNG HUI LIN, G. DIERSSEN, S. MINGRINO, and I. S. COOPER. *Archives of Neurology* [*Arch. Neurol.*] 3, 267–270, Sept., 1960. 5 refs.

The authors set out to provide evidence in support of views, previously based on empirical conceptions, concerning the selection for surgery of patients with Parkinsonism and the likelihood of achieving improvement thereby.

Of four groups of patients studied, the first (57 patients) had tremor, rigidity, and motor dysfunction confined to the extremities of one side, the condition being classified as unilateral Parkinsonism. Immediate good results were obtained with surgery in 91% of the patients; at follow-up examination 6 months to 4 years later of 40 of the patients the percentage showing good results was 75·8, there being spread of symptoms to the other side in some cases. The second group (100 patients) had mild or moderate symptoms, either unilateral or bilateral, but were fully self-sufficient and actively employed. All the patients in this group with early Parkinsonism were under 60 years of age and showed no mental deterioration or other physical defects. At the time of discharge from hospital the results of surgery were good in 90%; at follow-up examination of 85 patients the percentage with good results had fallen to 84·7, progression of the disease being observed in some of the cases. The third group (100 patients) had bilateral severe tremor, rigidity, bradykinesia, and motor dysfunction—that is, advanced Parkinsonism. The immediate results of surgery were good in 42%, and of 40 followed up, 44% showed good results. However, mortality was higher (5%) and permanent neurological deficit more frequent (4%) in this group than in the two previous groups (1% for each of these factors). In the fourth group, of 100 elderly patients with Parkinsonism (all aged over 60), the immediate results of surgery were good in 68; at follow-up examination of 70 patients results were considered to be good in 75%. However, postoperative mental confusion was a prominent complication in this group.

Thalamectomy was the most effective procedure for alleviation of tremor and rigidity, especially the former; it also improved over-all motor function as effectively as did pallidectomy and is therefore the treatment of choice. It is concluded that patients with unilateral and early Parkinsonism are good subjects for surgery and that patients with advanced disease are in general poor subjects, although in some instances the serious incapacity justifies the risks of surgical intervention.

J. V. Crawford

1058. Percutaneous Injection of the Thalamus in Parkinsonism: a Preliminary Report: Relief of Bilateral Facial Grimaces

A. ECKER and T. PERL. *Archives of Neurology* [*Arch. Neurol.*] 3, 271–278, Sept., 1960. 6 figs., 17 refs.

A new method of reaching the ventrolateral nucleus of the thalamus with a needle for destructive injection in Parkinsonism is described in this paper from the State University of New York Upstate Medical Center. In summary, the required spot is determined by measurements from the calcified pineal gland or, if this is not visible in radiographs of the skull, pneumoencephalograms are taken and the point calculated from the posterior commissure. The skull is penetrated through the foramen ovale as in injections of the Gasserian ganglion. A needle is sited under radiological control, a wire grid being used on the cheek to enable the correct entry point and bearing angle to be calculated. When the inner needle is in the calculated position 0·1 ml. of 1% procaine is injected two or three times. If tremor and rigidity are relieved then a mixture of absolute alcohol and sodium diatrizoate (5:1) is injected 0·1 ml. at a time. Further radiographs are taken to confirm the site of injection. Injections are continued until maximum benefit is obtained or complications ensue.

In 7 patients followed up for an average of 15 months contralateral rigidity and tremor were largely or completely relieved; in 2 of these patients there was also relief of involuntary bilateral movements of the lips and tongue. The authors consider that the method has the following advantages: (1) no general anaesthesia; (2) a burr-hole in the skull is avoided; (3) the very fine needle used to penetrate the brain minimizes the risk of haemorrhage in the basal ganglia; and (4) full exposure of the head permits accurate radiography. *J. V. Crawford*

1059. **Encephalographic and Clinical Investigations of the Functional Topography of the Pallidum Internum after Stereotactic Pallidotomy.** (Encephalographische und klinische Untersuchungen zur funktionellen Somatotopik des Pallidum internum bei stereotaktischen Pallidotomien)

F. MUNDINGER and P. POTTHOFF. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **201**, 151–164, 1960. 5 figs., 37 refs.

It is now well known that a circumscribed surgical lesion produced in the globus pallidus internus by electrocoagulation results in symptomatic relief of the tremor and rigidity in Parkinsonism. After the globus pallidus has been located radiographically by reference to certain bony structures various lesions are produced with the help of a stereotactic instrument and the clinical effect, such as decreased rigidity, observed. It has been shown that this decrease may be limited to the head and shoulders, the upper extremities, or the lower extremities. In 92 cases treated by this procedure at the University Neurological Clinic, Freiburg-im-Breisgau, the site of the lesion was compared with the clinical effect produced. It was found that the body schema head–arm–leg is represented in the globus pallidus in a rostro-dorsal direction. This finding thus permits of the possibility of choosing the site of the surgical lesion so as to effect that part of the body which shows maximum rigidity.

J. Hoenig

PERIPHERAL NERVES

1060. **Paralytic Brachial Neuritis. Discussion of Clinical Features with Review of 23 Cases**

K. R. MAGEE and R. N. DEJONG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 1258–1262, Nov. 5, 1960. 8 refs.

The authors review the clinical features of 23 cases of paralytic brachial neuritis seen at the University of Michigan Medical Center, Ann Arbor. Of the 23 patients, 21 were males; this high ratio is consistent with other reported series. The ages ranged from 8 to 64 years, but the disease was most common in the third and fourth decades. In 5 cases acute respiratory infection preceded the illness; one patient had been receiving treatment for neurodermatitis and one complained of malaise before the paralysis occurred.

The illness is characterized by severe pain about one or both shoulders at the onset, and within hours or days weakness of the muscles around the shoulder-joint develops. It is difficult to fix the exact time of onset of the paralysis, as pain prevents movement of the affected shoulder. The affected muscles may atrophy; fasciculation is rare, but sensory loss may occur. The pattern of motor and sensory loss follows the distribution of a peripheral nerve or nerve root. The deltoid, supraspinatus, and intraspinatus muscles are those most frequently involved. Radiography of the spine in 19 cases showed no abnormality beyond osteoarthritis compatible with the age of the patient. In one case the protein content of the cerebrospinal fluid was 98 mg. per 100 ml. and in 2 others 51 and 53 mg. per 100 ml. respectively; otherwise findings in the 7 cases examined were normal.

Recovery may begin within a few days of the paresis, and the prognosis is generally good. Complete recovery, however, may take 3 to 6 years in individual cases. In diagnosis poliomyelitis has to be considered. The absence of constitutional symptoms and the presence of sensory changes are important points in the differential diagnosis. No aetiological agent has yet been identified, and there is no specific treatment. Analgesics are required for the pain in the early stages, and a full range of movements of the shoulder-joint is advocated from the beginning. *William Hughes*

1061. **Femoral Neuropathy**

J. R. CALVERLEY and D. W. MULDER. *Neurology* [*Neurology (Minneap.)*] **10**, 963–967, Nov., 1960. 23 refs.

Injury of the femoral nerve is an important cause of pain, loss of sensation, and weakness in the lower limb, and may frequently be a sign of serious systemic disease. In this paper the authors describe 19 cases of femoral neuropathy seen at the Mayo Clinic during 1957–9 and briefly review the various causes of this disorder as reported in cases previously described in the literature. These have included injury during abdominal and pelvic operations or during parturition, diabetes mellitus, haemophilia (in which a slight injury to the thigh was followed by prolonged bleeding and pressure on the femoral nerve), herpes zoster, diseases of the hip-joint, and benign as well as malignant tumours. Of their own 19 patients, 14 had diabetes mellitus and the authors consider that the femoral nerve dysfunction was the result of ischaemia due to acute alterations in the blood supply to the nerve. A further 3 patients had periarteritis nodosa, while in 2 cases no cause for the neuropathy could be discovered, although one of these patients gave a history of recent herpes zoster affecting the sciatic nerve region and he was also suffering from atherosclerosis and a femoral hernia. *J. B. Cavanagh*

NEUROMUSCULAR DISEASES

1062. **Changes in Serum Complement Activity in Patients with Myasthenia Gravis**

W. L. NASTUK, O. J. PLESCIA, and K. E. OSSERMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **105**, 177–184, Oct. [received Dec.], 1960. 2 figs., 10 refs.

Studies of the serum complement levels in myasthenia gravis are reported in this paper from Columbia University, New York, Rutgers University, New Brunswick, and the Mount Sinai Hospital, New York. Estimations of serum complement activity were made with a carefully standardized haemolytic system. Values for the test sera were expressed in terms of that obtained for a standard serum obtained from a healthy individual and stored at −35° C. This standard was titrated in parallel with each batch of test sera. [The original paper should be consulted for technical details.]

Values obtained with test sera from a control group of 13 healthy subjects ranged from 0·8 to 1·2 units of activity, with a mean of 1·0 unit. Sera from 68 patients with myasthenia gravis were tested, one estimation being made in 22 cases and 2 or more serial observations made over periods of one week to 44 months in 46. The values were distributed over a wide range (0·05 to 2·57 units) and were below the normal range in 40 cases and above normal in 31. Of the 68 patients, 54 at some time gave values lying outside the normal range.

In 22 cases clinical correlation was not possible for a variety of reasons. The remaining 46 patients were divided into 3 groups according to the severity of the disease and an attempt was made to correlate the clinical condition with the serum complement values. Of 15 patients in whom the disease was increasing in severity, 11 had low, 3 high, and one normal serum complement activity. Of 21 patients in whom there was evidence of a remission, 17 showed a rise of serum complement activity to normal or supernormal levels and 4 showed no significant change or a slight fall. Of 14 patients in whom the clinical condition was constant, 6 gave values within the normal range and showing little variation, the remainder having variously low, normal, or elevated values. [Details of the values in these groups of patients are not given.]

The authors conclude that there is a correlation between serum complement values and the activity of the disease process, the values tending to be lowest during exacerbations and returning to normal or supernormal levels with remission. They suggest that the results obtained are consistent with the hypothesis that a complement-fixing antigen–antibody reaction occurs *in vivo* in myasthenia gravis and that an autoimmune mechanism may be of some importance in the aetiology of this disease. *Hewett A. Ellis*

1063. **Immunofluorescence Demonstration of a Muscle Binding, Complement-fixing Serum Globulin Fraction in Myasthenia Gravis**
A. J. L. Strauss, B. C. Seegal, K. C. Hsu, P. M. Burkholder, W. L. Nastuk, and K. E. Osserman. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **105**, 184–191, Oct. [received Dec.], 1960. 6 figs., 8 refs.

This paper from Columbia University and Mount Sinai Hospital, New York, and the New York Hospital–Cornell Medical Center describes the application of immunofluorescent techniques to the investigation of the hypothesis that an autoimmune phenomenon occurs in myasthenia gravis [see Abstract 1062]. Two types of experiment were carried out with the object of demonstrating (1) the presence of a muscle-binding globulin in the serum of patients with myasthenia gravis and (2) the ability of this globulin (when already bound to muscle) to fix complement subsequently added.

In the first group of experiments 2 globulin fractions, prepared by precipitation with sodium sulphate from pooled sera from 10 patients with myasthenia gravis and from 12 healthy subjects respectively, were conjugated with fluorescein *iso*cyanate and used in attempts to "stain" sections of various fresh muscle preparations. It was observed that the myasthenic globulin conjugate "stained" alternate striations of skeletal muscle sections, whether the muscle was obtained from myasthenic or normal subjects, but gave negative results with cardiac and smooth muscle. Normal globulin conjugate gave negative results with all types of muscle. Preliminary treatment of the skeletal muscle sections with unconjugated myasthenic globulin or with whole serum from 13 individual myasthenic patients prevented the "staining" of the striations on subsequent addition of conjugated myasthenic globulin. Similar preliminary treatment of the sections with normal unconjugated globulin or with whole serum from normal subjects did not inhibit the reaction.

In the second series of experiments sections of human skeletal muscle treated with unconjugated myasthenic globulin and then with guinea-pig serum complement were tested for the presence of bound complement by adding fluorescein-conjugated rabbit anti-guinea-pig complement antiserum. Positive results were obtained when this system was used with normal and myasthenic skeletal muscle and also in 8 out of 10 cases when sera from the myasthenic subjects used in the original serum pool were substituted for the unconjugated myasthenic globulin. When sera from 11 normal subjects were tested in the same way they gave negative results.

The evidence obtained from these experiments provides additional support for the hypothesis that a serum complement-fixing immune reaction occurs in myasthenia gravis. *Hewett A. Ellis*

1064. **The Effect of Haemodialysis in Myasthenia Gravis**
E. Stricker, H. Thölen, M. A. Massini, and H. Staub. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 291–294, Nov., 1960. 8 refs.

Haemodialysis was performed over periods of 8 to 20 hours in a group of 8 myasthenic patients at the University Medical Clinic, Basle. This was undertaken on the assumption that some chemical neuromuscular blocking agent is present in the blood in this disease. Temporary improvement followed this procedure in 5 cases, as shown by amelioration of symptoms and signs and reduced need for anticholinesterase drugs.

The authors discuss possible explanations of this improvement and give reasons for dismissing from consideration overdosage with anticholinesterase drugs, ionic alterations, and psychological factors or factors attending the procedure other than the dialysis. They conclude that the beneficial effect is best explained on the hypothesis that the dialysis removes from the body a substance of low molecular weight which has a neuromuscular blocking action. *J. B. Stanton*

1065. **Myasthenia Gravis in a Southern Community**
M. Alter, O. R. Talbert, and L. T. Kurland. *Archives of Neurology* [*Arch. Neurol.*] **3**, 399–403, Oct., 1960. 2 figs., 5 refs.

Psychiatry

1066. Psychotic Reactions after Cosmetic Operations. (Psychotische Reaktionen nach kosmetischer Operation) E. RINGEL. *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* [*Wien. Z. Nervenheilk.*] **18**, 51–63, 1960. 9 refs.

In this paper from the University Psychiatric Clinic, Vienna, attention is drawn to certain psychiatric complications which may follow cosmetic operations and which can often be predicted from the results of a psychiatric examination before the operation. This may reveal the following findings. (1) A neurotic reaction to the bodily defect, as described by Adler; in these cases improvement in the psychic state may be expected to be proportionate to the success of the operation. (2) A neurosis as well as the bodily defect. Here the abnormal attitude undergoes a development which later involves the whole personality and the neurosis becomes independent of the bodily defect itself; in such patients the operation should be preceded and followed by psychotherapy. (3) A neurosis which the patient attributes to the real (or even an imagined) bodily defect; such patients will certainly need intensive psychotherapy before the operation, but in fact in many cases the operation may never be carried out, as the patient may, after successful psychotherapy, no longer have the wish for it. (4) A psychotic reaction together with bodily defects, a condition described by Kretschmer ("sensitive delusions of reference"); in these cases the operation, even if successful, will fail to remove the psychosis. (5) It may be found that the feeling of "ugliness" or deformity which leads the patient to express a wish for operation may itself be a symptom of a depressive psychosis.

The author describes 2 cases in which a depressive psychosis was precipitated by a successful cosmetic operation, a so-called "paradoxical reaction", which is explained in terms of pre-morbid psychogenic abnormal development. He concludes with a plea for close co-operation between surgeon and psychiatrist.

J. Hoenig

1067. Transvestism. (Transvestitismus.) [Review Article]
G. HOFER. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **29**, 1–33, Jan., 1961. Bibliography.

1068. Obstetric and Social Origins of Mentally Handicapped Children
D. V. I. FAIRWEATHER and R. ILLSLEY. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 149–159, Oct., 1960. 25 refs.

With the help of health and educational authorities the authors identified, during 1958, 66 out of an estimated total of 87 mentally handicapped children born in Aberdeen in 1948, the loss of the remaining 21 being attributed mainly to migration. The criterion of mental handicap was that used by the local education authorities, namely, an I.Q. of 70 or less, except that 5 children with an I.Q. slightly over 70 who were attending a special school because of poor educational progress were included.

Of these 66 children, 3 had died before 1958 and 4 were known to have left the city. In 58 out of the remaining 59 cases details of personal and family history were obtained directly from the mother, and in all 66 cases pregnancy and labour records were examined for abnormalities which might have damaged the child. Such abnormalities were present in 8 cases, in one of which a difficult forceps delivery "was undoubtedly the cause of cerebral damage", while in the 7 others the link between obstetric abnormality and mental handicap was conjectural. In 12 cases the child's birth weight was 5½ lb. (2·5 kg.) or less, and the incidence of prematurity in the group was 16·9% compared with a rate of 5·6% for the city as a whole. In 21 cases there was also a physical defect or a history of a possibly relevant illness. In 58 families studied there was a high frequency of marital and occupational instability (30), of poor social conditions (39 mothers had been unskilled or semi-skilled workers), of high fertility (mean family size 4·7 compared with 3·3 for Scotland), and of low average intelligence.

From the results of this investigation it is concluded that the direct contribution of obstetric complications to the total of mental handicap is small compared with familial factors, and it is suggested that the high incidence of such complications in the obstetric history of mentally handicapped children is largely the indirect result of their association with poor maternal physique and health, which are themselves related to poor social conditions and low intelligence.

F. T. H. Wood

1069. An Endocrine Study of Depressive Illness
J. L. GIBBONS, J. G. GIBSON, A. E. MAXWELL, and D. R. C. WILLCOX. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **5**, 32–41, Sept., 1960. 5 figs., 19 refs.

The authors have investigated some aspects of the natural course of depressive illness from the point of view of thyroid and adrenocortical activity by means of a study of 21 depressive illnesses in 17 male patients admitted to the Metabolic Ward of the Maudsley Hospital, London. All the patients were severely depressed, with a history of major symptoms lasting 10 days to 6 months. Their mean age was 45·7 years. Three patients recovered without physical treatment and 18 were treated with electric convulsion therapy (E.C.T.), to which 13 responded promptly. Successive 24- or 48-hour urine specimens were collected and serial estimations made of the excretion of creatinine, total neutral 17-ketosteroids (17-KS), and acid-stable formaldehydogenic substances

(A.S.F.S.), a measure of glucocorticoid excretion. Thyroid function was assessed by estimation of serum protein-bound iodine (P.B.I.) content at weekly intervals (13 patients) or during the first week in hospital (5 patients). In 9 patients the neck–thigh ratio of ^{132}I activity was also estimated.

In all the patients on whom serial observations of the serum P.B.I. level were made the mean values were within the normal range, the mean for the whole group being 4·8 μg. per 100 ml. (normal mean 5·0 μg. per 100 ml.). The variation in weekly values in individual patients rarely exceeded 1 μg. per 100 ml. except in 2 cases in which it was more than 2 μg. per 100 ml. Comparison of the mean values for the first and last estimations of serum P.B.I. level showed a small, but statistically significant, decrease (0·5 μg. per 100 ml.) which the authors judge to be of doubtful clinical significance. Variations in adrenocortical function, as assessed by 17-KS and A.S.F.S. output, were more striking, 8 patients out of 19 giving numerous 17-KS values above the upper limit of normal for their age and 16 patients giving high values for A.S.F.S. excretion, while there were day-to-day and longer-term fluctuations in the values in every case. Further examination of these data suggested: (1) that there was no consistent relationship between steroid excretion and the general course of the illness, although there was some association in certain individual patients; (2) that no consistent effect on steroid excretion was attributable to E.C.T.; (3) that the presence of anxiety or agitation was associated with an increase in corticoid excretion; and (4) that particular preoccupations with a sexual content were associated with an increase in 17-KS excretion.

In an attempt to detect evidence of a regular cycle of adrenocortical activity data from 5 patients were examined by means of variograms and a 72-day series of observations on one patient was submitted to Fourier analysis. From the first of these investigations evidence of 5- to 12-day cycles was obtained and in the second there was tentative evidence of a 7-day cycle. These cycles, if present, appear to be of very low amplitude and of uncertain clinical significance. *R. H. Cawley*

1070. **Clinically Important Laboratory Findings in Idiopathic Schizophrenia.** (Klinischwichtige Laboratoriumsbefunde bei der idiopathischen Schizophrenie)
H. H. Fleischhacker. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **201**, 1–16, 1960. 47 refs.

The author reports that the laboratory examination of the various body fluids in a group of patients [number not stated] with confirmed schizophrenia revealed the following abnormalities of clinical significance in diagnosis. The urine showed toxicity for certain micro- and macro-organisms, and in very acute cases of the disease a positive glyoxylic acid reaction. In the blood there was a slight rise in the serum γ-globulin level. The cerebrospinal fluid showed a slight rise in protein content, mainly due to an increase in the γ-globulin fraction, and a slight increase in the number of cells. These findings [for which no numerical values are reported] are in no way specific. Their significance is discussed and it is suggested that they may be due to: (1) the "schizoid" constitution; (2) the local effects of the schizophrenic lesion, whatever that may be; (3) the "schizophrenic process" itself [as nothing is known about this process this hypothesis is not even debatable]; or (4) an increase in the level of antibodies in the blood serum and spinal fluid. The importance of the findings for further research in schizophrenia is stressed and similar findings reported in the literature are reviewed.

J. Hoenig

1071. **Deterioration after Electroconvulsive Therapy in Patients with Intracranial Meningioma**
M. M. Gassel. *Archives of General Psychiatry* [*Arch. gen. Psychiat.*] 3, 504–506, Nov., 1960. 8 refs.

Psychiatric symptoms are sometimes the presenting feature in cases of intracranial tumour, and the potential danger of treating these with electric convulsion therapy (E.C.T.) is underlined by this paper from the National Hospital, Queen Square, London. Reviewing the records of 250 consecutive cases of intracranial meningioma, the author found 3 cases which had previously been given E.C.T. for psychiatric symptoms. The first patient had a history of 10 months' headaches and vomiting, and when first seen was thought to be suffering from a depressive stupor. After a course of E.C.T. abnormal physical signs appeared, including drowsiness and confusion, bilateral papilloedema, unequal pupils, and bilateral extensor plantar responses. A right fronto-temporal meningioma was diagnosed and was removed surgically. The second patient had headaches and vomiting for 9 months, sometimes followed by bouts of wild, uncontrollable behaviour. On admission to a mental hospital she became talkative and hyperactive, but the only abnormal physical finding was an indeterminate right plantar response. A diagnosis of "hyponeuria" was made and she was given E.C.T. on 4 occasions within a week. After the last treatment she became drowsy and unresponsive; there were right miosis, bilateral papilloedema, and spasticity of the lower limbs with bilateral extensor plantar responses. Investigation revealed a large cystic right parieto-occipital meningioma. The third patient developed slowness of speech, found her work too much, was clumsy in her right extremities, and became depressed. She was given E.C.T. on 4 occasions at 5-day intervals, after which she had a memory disturbance, aphasia, papilloedema, a right hemiplegia, and other signs. A large left parietal parasagittal meningioma was found and was partially removed.

The author maintains that the E.C.T. caused the deterioration noted in all 3 cases. No abnormal physical signs had been discovered in any patient before E.C.T. was given. A review of the literature disclosed 4 other reports of similar deterioration in patients after E.C.T. prescribed before an intracranial tumour was suspected. Such deterioration, the author suggests, may be due to changes in vascular and cellular permeability resulting in enlargement of the tumour, and he concludes that where an intracranial tumour is suspected E.C.T. is contraindicated. *J. S. Bearcroft*

Dermatology

1072. **The Treatment of Lichen Planus with Dipasic**
J. O'D. ALEXANDER. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 355–357, Oct., 1960. 1 ref.

Lichen planus is often very resistant to treatment and many, even some bizarre, forms of therapy have been employed. The present author, having learned from a colleague that a strongly positive Mantoux reaction had been observed in a patient with this disorder, has tried, at Glasgow Royal Infirmary, the effect of " dipasic ", the *para*-aminosalicylic acid salt of *iso*nicotinic acid hydrazide, in the treatment of 41 patients, a further 15 being given a placebo tablet. The average period of treatment was 3 months, and the dosage was arbitrarily fixed at 600 mg. daily for 6 weeks followed by 300 mg. for a further 6 weeks; no local therapy was given during the trial. Of the 41 patients, 26 were cured and 6 greatly improved, while 5 showed some improvement of varying degree and 4 no change; of the controls, 5 showed good spontaneous improvement and 8 no change. Analysis of the results by type of the disorder revealed that lesions of the acute type or small local lesions responded best, while hypertrophic lichen planus and mucosal lesions failed to improve. No toxic effects were observed. The mechanism of action of dipasic is not known and the author does not claim it as a specific treatment for this disease.

[It is doubtful whether the results recorded are much of an improvement on those obtained with other methods of therapy, but further trials seem justified, if only to determine the mode of action.] *Allene Scott*

1073. **Electron Microscope Observations on the Human Wart.** [In English]
A. CHARLES. *Dermatologica* [*Dermatologica (Basel)*] **121**, 193–203, Oct., 1960. 5 figs., 25 refs.

This paper from the University of Leeds describes work undertaken to support the evidence of the viral origin of human warts. The findings are based on the electron microscopy of two warts, and the paper is illustrated with labelled electron-photomicrographs. These show the presence in the nuclei of particles about 33 mμ in diameter which are arranged in the strikingly orderly fashion associated with viral crystals. Some of the particles are dispersed and scattered around the nucleus, but there is no difficulty in distinguishing them from the granular material of the nucleoplasm. It was not possible to make out any internal structure in the particles.

In his discussion the author compares the human wart virus with that of the rabbit papilloma (Shope), which is closely analogous but which shows some indication of a non-specific internal structure. Other groups of viruses which develop in the nucleus are the herpes virus and the RI–APC group of viruses, said to be responsible for certain acute respiratory diseases, epidemic keratoconjunctivitis, and pharyngo-conjunctival fever. These, however, appear to have much larger particles (about 60 mμ) with more marked internal differentiation.
Benjamin Schwartz

1074. **Vitamin C and Exfoliative Dermatitis**
A. TICKNER and A. BASIT. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 403–408, Nov., 1960. 2 figs., 9 refs.

As part of an investigation being carried out at St. John's Hospital for Diseases of the Skin, London, into exfoliative dermatitis, ascorbic acid saturation tests were performed on 26 patients with exfoliative dermatitis, 12 with eczema, 13 with psoriasis, 8 with varicose ulcers or eczema, and 25 healthy control subjects. The saturation time (normal $1{\cdot}7 \pm 0{\cdot}84$ days) was prolonged in all patients except those with varicose ulcer, and was particularly increased in those with exfoliative dermatitis (up to 10·4 days). Blood ascorbic acid levels, determined in 10 patients with exfoliative dermatitis and 2 normal subjects, were initially low in those with exfoliative dermatitis, but started to rise as soon as vitamin C was given, thus confirming that the prolonged saturation times in these patients did not result from malabsorption of ascorbic acid from the intestine. No aetiological relationship between vitamin C and exfoliative dermatitis is implied, but since it appears that the requirements of vitamin C are increased in this condition, it is suggested that an adequate supply should be made available to these patients. The excretion of tyrosyl derivatives after the administration of tyrosine was also investigated, but only confirmed previous results. *G. W. Csonka*

1075. **Sensitivity to Hydrocortisone Acetate Ointment**
R. CHURCH. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 341–344, Oct., 1960. 2 refs.

With the introduction of ointments containing hydrocortisone acetate for the treatment of eczematous conditions of the skin it was thought that a rational form of therapy free from the danger of sensitization had at last been achieved, but recently there have been several reports of apparent allergy to the hydrocortisone itself. At the Royal Infirmary, Sheffield, 5 such cases seen in the space of 10 months were investigated to determine the exact nature of the allergy. It was discovered that these patients were allergic only to two proprietary brands of hydrocortisone acetate ointment (Brands W and Z) and showed no reaction to another type of hydrocortisone ointment (Brand X) or to the bases in which it was incorporated. It was therefore considered that possibly one of the intermediate products of steroid manufacture might be the source of the trouble. Patch tests with " steroid intermediate " [not identified chemically] and with 21-diol acetate (a precursor of hydrocortisone acetate), which were found to be produced during the production of the hydrocortisone used in Brands W and

Z, demonstrated that it was to these ingredients, particularly the 21-diol acetate, that the patients were allergic; these intermediary contaminants were present in small quantities in the final preparation of Brands W and Z owing to incomplete catalysis. The author points out that the incidence of such sensitization is probably very small, since thousands of patients have been treated with the same ointments without developing signs of sensitivity. *Allene Scott*

1076. ***Trichophyton sulphureum* in a Residential School**
D. W. R. MACKENZIE, D. BURROWS, and A. L. WALBY. *British Medical Journal* [*Brit. med. J.*] **2**, 1055–1058, Oct. 8, 1960. 3 refs.

The finding in the summer of 1959 of infection with *Tricophyton sulphureum* in 7 girls at a residential school in Belfast led to an investigation of the incidence of the infection among the total of 128 female pupils. It was known that in 1955 there had been 5 cases of ringworm in the school; 2 of the affected children were still resident and one of these had been treated with Whitfield's ointment and had probably remained infective. Sampling techniques showed that *T. sulphureum* could be recovered from many non-living sites, such as hair-brushes and pillow-slips, in contact with children not ostensibly infected as well as those who were infected. It was also recovered from floors, lockers and bedding, and aerial spread was demonstrated. Investigation showed that 20 children were infected, although none showed a marked inflammatory response. Lesions on the body were usually single, erythematous patches with little scaling, while scalp lesions consisted of seborrhoea-like scaly patches.

In treatment griseofulvin was given by mouth together with topical application of a fungicidal ointment. The response was slow, although clinical improvement was usually evident after two weeks. Experience showed that four successive negative cultures were required before treatment could be stopped. All non-infected children were given griseofulvin prophylactically in a dosage of 50 mg. daily (one-fifteenth the therapeutic dose), and non-living sources of infection were sterilized or removed. The authors state that clinical detection was difficult, some of the cases being discovered up to 6 months after the first examination. However, eradication of infection appeared almost complete; all non-living sources were eradicated and all except one of the children were cured, the exception being isolated from school until the criterion for cure was satisfied.

E. H. Johnson

1077. **Intensive Griseofulvin Therapy in Tinea Capitis.** [In English]
F. REISS, L. KORNBLEE, and R. GIBBS. *Dermatologica* [*Dermatologica (Basel)*] **121**, 257–264, Nov., 1960. 6 refs.

Previous reports have shown that fungus infections of the scalp could usually be cured by the oral administration of 0·5 to 1 g. of griseofulvin daily for 6 weeks, although some patients required more prolonged treatment. In the study here reported from Bellevue Hospital, New York, an attempt was made, in view of the low toxicity of the drug, to shorten the duration of therapy by employing larger doses. A daily dose of 4 g. was therefore given for one to 5 weeks to 15 male patients aged 4 to 12 years with tinea capitis, due in 14 cases to *Microsporum audouini* and in one to *Trichophyton tonsurans*. Cure was obtained in 3 weeks in 11 patients, 2 required 4 weeks, and one 5 weeks, the remaining patient being lost to observation. Albuminuria occurred in 6 cases, being marked in one after 84 g. of the drug had been given over 3 weeks, but in the remainder it was slight. In all cases it was transient and no other significant side-effects were noted. In an addendum to their paper the authors state that a single daily dose of 3 g. of griseofulvin was used in the treatment of a further 6 patients with infection of the scalp due to *M. audouini* and that 5 were cured in varying periods. *R. R. Willcox*

1078. **The Treatment of Onychomycosis with Griseofulvin**
G. K. HARGREAVES. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 358–364, Oct., 1960. 7 refs.

Onychomycosis, particularly that due to *Trichophyton rubrum*, has, as might be expected, proved the most difficult of attack by griseofulvin. In an attempt to assess the ancillary effect of surgical avulsion of the nails in treatment the results in two groups of patients attending the General Infirmary at Leeds were compared. The first group (17 patients) with fungus infection of both finger- and toe-nails were treated by avulsion followed by 1 g. of griseofulvin daily for an average period of 4 months; of these, 14 were infected with *T. rubrum*, 2 with *T. mentagrophytes*, and one with both fungi. The second group, of 16 patients all infected with *T. rubrum*, were given the same dosage of griseofulvin for periods ranging from 6 to 12 months, that is, until two negative cultures had been obtained. In both groups all skin lesions had cleared entirely within 2 weeks and affected palms and soles were normal in 6 to 8 weeks. Interdigital maceration often persisted, however, although cultures from these areas were negative. The results of treatment of finger-nails were satisfactory in both groups, and the existence of other nail disorders (such as pityriasis rubra pilaris) did not appear to hinder the response. The only toxic effects noted were occasional headache and a temporary slight fall in the leucocyte count.

From the author's discussion four interesting points emerge. (1) While avulsion does not materially accelerate the improvement in infected finger-nails, which do well in any case, toe-nails do clear more quickly if avulsion is carried out beforehand; it would seem that the slow rate of growth of the toe-nails and their differing circulatory characteristics have an important effect in limiting the response—thus with avulsion 2 months was sufficient to produce non-infected toe-nails, whereas in the patients given griseofulvin alone some nails had not cleared in 12 months. (2) The prolonged therapy necessitated in the latter situation gives time for development of resistance of the fungus to griseofulvin. (3) The observed frequency of superimposed infection with *Candida albicans* in the healing nail, which fortunately however could be well controlled with nystatin. (4) The author

makes the interesting observation in support of long-term therapy in place of the short, quick, courses occasionally proposed, that with intermittent or short-term therapy the soft periungual keratin is open to reinfection from the more slowly discarded hard keratin of the nail, which is still carrying the fungal elements.

Allene Scott

1079. **The Successful Treatment of Behçet's Syndrome with Dapsone.** (Успешное применение диаминодифенил-сульфона при болезни Бехчета)
M. S. Bragin. *Вестник Дерматологии и Венерологии* [*Vestn. Derm. Vener.*] **34**, 65–67, Nov., 1960. 7 refs.

A case of Behçet's syndrome is described in which the patient, a woman of 35, had genital and oral ulcers, iritis, and arthritis. Cortisone produced only temporary improvement followed by an exacerbation.

Treatment with dapsone (DDS) was then started in a dosage of 0·05 g. twice daily, 3 courses, each of 6 days' duration, being given. The patient's condition improved and the iritis and joint symptoms gradually disappeared. She still has occasional ulcers of the mouth. A second patient was cured after only one 6-day course of DDS. The author suggests that the rapid regression of clinical signs following treatment with DDS substantiates the theory of the infective aetiology of Behçet's disease.

N. Hopewell

1080. **A Comparative Study of the Treatment of Staphylococcal Skin Infections by Electrophoresis with Various Drugs.** (Сравнительная оценка лечения стафилодермий электрофорезом различных лекарственных веществ)
M. I. Karlin, G. Ja. Klebanov, and A. S. Provotorova. *Вестник Дерматологии и Венерологии* [*Vestn. Derm. Vener.*] **34**, 26–27, Nov., 1960.

The electrophoretic application of penicillin in staphylococcal skin infections having, it is claimed, proved successful, the authors have used the same method with staphylococcal antiphage, 10% aqueous solution of ichthyol, and 10% aqueous solution of potassium iodide. The technique is as follows. A compress is applied to the skin, soaked with the solution to be used, and attached to the negative electrode, the strength of the current being varied according to the area of the body treated. The best results were obtained when potassium iodide was used. It would appear that electrophoresis allows for deeper penetration of the skin by the drug than with topical application, and so increases its effect.

N. Hopewell

1081. **Edathamil in the Treatment of Scleroderma and Calcinosis Cutis**
P. R. Winder and A. C. Curtis. *Archives of Dermatology* [*Arch. Derm.*] **82**, 732–736, Nov., 1960. 2 figs., 15 refs.

From the University of Michigan Medical School, Ann Arbor, the authors report the results obtained with the chelating agent sodium calciumedetate (sodium salt of ethylenediaminetetraacetic acid) in the treatment of 27 cases of scleroderma in patients aged 7 to 75 years. All the patients were admitted to hospital and given the agent intravenously over a period of 4 to 6 hours daily for 15 days, 14 of them receiving one such course, 6 two courses, 6 three courses, and one four courses. The daily dosage varied from 200 mg. in 200 ml. of 5% dextrose solution in the youngest patient to 3 g. in 500 ml. 5% dextrose in the adults.

The results were not spectacular, 7 of 19 patients with acrosclerosis being objectively improved, 4 " questionably improved ", and 8 unchanged, while of 3 patients with linear scleroderma, one was questionably improved; there was also some improvement in single cases of generalized morphoea, localized morphoea, and morphoea-like changes in porphyria cutanea tarda. One of the 2 patients with calcinosis cutis also improved. In regard to side-effects, burning at the infusion site was common, nausea and anorexia occurred in 2 cases, and one patient developed renal irritation with albuminuria and granular casts. The side-effects became less marked when the rate of infusion was slowed. The authors suggest that the use of sodium calciumedetate in the treatment of systemic scleroderma seems to be justified, although " the ultimate usefulness of the drug is still to be appreciated ".

Benjamin Schwartz

1082. **The Natural History of the Strawberry Nevus**
R. E. Bowers, E. A. Graham, and K. M. Tomlinson. *Archives of Dermatology* [*Arch. Derm.*] **82**, 667–680, Nov., 1960. 11 figs., 22 refs.

The term " strawberry naevus " is used here to describe the common cutaneous angioma of infancy or cavernous haemangioma composed of large blood vessels and blood-filled spaces. The authors discuss previous reports in the literature relating to the management of these lesions and describe in some detail their natural history with reference to a series of 140 untreated cases (169 naevi) followed up for at least 5 years in the north Gloucestershire area. The results are illustrated graphically and photographically.

Complete spontaneous resolution was observed in approximately 50% (82) of the naevi by the time the patient reached the age of 5 years and 70% by the age of 7. Continued improvement was noted in other cases after this age and has been reported to occur even in teenage children. The size of the naevi, the fact that they were multiple, and the sex of the child apparently had no relationship to the speed of resolution, and in general the site was also unimportant, except that lesions of the lip seemed to resolve less satisfactorily. Early extension of a naevus was frequently noted, but none enlarged after 12 months from its first appearance and no significant damage to surrounding tissues occurred in any of the cases. It was noted, however, that early diminution in size of the naevi did not always lead to early cure, but if a lesion had not improved by the end of the 3rd year it was unlikely to have recovered completely by the 7th. No serious haemorrhage was seen, and ulceration, which occurred in some of the larger lesions, did not significantly change the course. There was no evidence to suggest that naevi occur more often in premature babies. Of the 42 naevi which remained

uncured, some were still improving at the end of the survey, while in 28 cases there were residual angiomata, 6 with some scarring, but 14 had only residual telangiectasia. It is suggested that simple surgical treatment is likely to be adequate in any case in which the residual lesion is likely to result in cosmetic handicap. The authors note in an addendum that their results are very similar to those recently reported by Simpson (*Lancet*, 1959, **2**, 1057). *Benjamin Schwartz*

1083. **The Treatment of Mycosis Fungoides with a New Agent, Cyclophosphamide (Cytoxan)**
D. C. ABELE and R. L. DOBSON. *Archives of Dermatology* [*Arch. Derm.*] **82**, 725–731, Nov., 1960. 9 figs., 5 refs.

Cyclophosphamide (" cytoxan ") has been used with varying success in the treatment of tumours and malignant haematological conditions. In view of its theoretical advantages an evaluation of its usefulness in mycosis fungoides was undertaken at the University of North Carolina School of Medicine, Chapel Hill.

The case histories of the first 4 patients treated (2 white and 2 negro males) are given in detail. All were in the premycotic or infiltrative stage and none had tumour. The dosage regimen eventually evolved showed that initial treatment with 200 mg. of cyclophosphamide daily for 14 to 21 days produced optimum results with minimum side-effects. The subjective symptoms usually subsided in 4 to 7 days and the exfoliation cleared, with thinning of infiltrated plaques, in 10 to 14 days. Moderate alopecia was the only side-effect noted at this time. After this initial treatment the resulting remission was maintained by means of a single weekly dose of 400 to 700 mg. of the drug. If this rather large dose caused nausea or vomiting half of it was given in the middle of the week, but with apparently less satisfactory control of the disease. No other side-effects were noted, although leucopenia was expected. The authors were impressed with the value of cyclophosphamide in the treatment of mycosis fungoides and consider that further trials of the agent would be justified. *Benjamin Schwartz*

1084. **Dihydroxyacetone (DHA). A Keratin Coloring Agent**
S. BLAU, N. B. KANOF, and L. SIMONSON. *Archives of Dermatology* [*Arch. Derm.*] **82**, 501–503, Oct., 1960. 2 figs., 6 refs.

The authors describe their experience with dihydroxyacetone (DHA), a degradation product of glucose, which has come to be widely used cosmetically because of its ability to " tan " human skin. It has long been recognized that combinations between groups of proteins or amino-acids and the aldehydes of sugars and their degradation products may result in the formation of a brown end-product, the structure of which is not yet known. Using DHA in a 4% alcoholic solution the authors carried out prophetic patch tests on the skin of 200 subjects, the reaction being read at 48 and 72 hours and the test repeated two weeks later. Apart from tanning of the test site no signs of primary or allergic reactions were noted. In 25 subjects the solution was applied to the face and other skin areas on alternate days for a period of 30 days; there was a gradually deepening yellow-brown coloration of the skin, which could not be washed off and lasted 5 to 15 days, but no evidence of primary irritation or allergic sensitivity. No cross-reactivity was observed in 12 patients giving a positive reaction to *para*phenylenediamine. Histologically, no inflammatory reaction was seen and the colour did not screen ultraviolet radiation.

It is suggested that DHA may be used as a cover in vitiligo, post-versicolor depigmentation, poikiloderma of the neck, melanosis of the face, and to hide other blemishes and depigmentations. *Benjamin Schwartz*

1085. **Dihydroxyacetone: a Suntan-simulating Agent**
H. I. MAIBACH and A. M. KLIGMAN. *Archives of Dermatology* [*Arch. Derm.*] **82**, 505–507, Oct., 1960. 3 refs.

The sun-tan properties and the effect on the skin of dihydroxyacetone (DHA) [see Abstract 1084] were studied at the Department of Dermatology, University of Pennsylvania. DHA is an intermediate in the metabolism of carbohydrates in higher plants and animals. It is very soluble in water, ether, alcohol, and acetone, is stable under normal conditions of storage, and large doses by mouth are well tolerated. On application to the skin a brownish colour develops after a few hours, which deepens proportionately when the strength of the solution is increased from 5% to 30%; concentrations above 30% tend to produce unnatural skin coloration.

Observations on 35 subjects showed that in general the depth of the colour varied directly with the thickness of the stratum corneum, the palms and soles staining deepest and the face being relatively less susceptible. Hard keratin—for example in the nails—was not darkened by routine use. Histologically, the colour did not penetrate deeper than the horny layer and melanin was not increased. The colouring was of no value as a sun screen and could be removed only by abrading the stratum corneum. In studies *in vitro* the reaction was found to be dependent on temperature—the higher the temperature, the more quickly the colour was produced. The reaction was the same in the *p*H range 4 to 8·6 and occurred similarly in total darkness and bright sunlight. Chemical tests showed that all protein materials could be darkened by DHA and that the reaction also occurred *in vitro* with a strongly alkaline solution. A variety of fats and carbohydrates did not stain. Since the brown colour could be totally inhibited by formalin it is suggested that the colour is the result of interaction between DHA and the amino groups of proteins.

Varying concentrations of DHA were applied daily to the skin of 15 patients (8 white and 7 negro) with vitiligo. A 2% solution seemed optimum for the hands and a 5% solution for general application in white patients; in negroes a concentration up to 30% was necessary and even then it was difficult to match the normal colour. Staining was frequently uneven, and speckling and mottling occurred; nevertheless, DHA proved a reasonably acceptable cosmetic for patients with vitiligo, none of whom showed any evidence of sensitization or irritation. *Benjamin Schwartz*

Paediatrics

1086. **Asian Influenza in Pregnancy and Congenital Defects**

R. Doll, A. B. Hill, and J. Sakula. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 167–172, Oct., 1960. 11 refs.

Influenza due to the Asian strain of virus A first became epidemic in Great Britain in the latter half of 1957 and spread rapidly. An inquiry into the incidence of the disease in a general practice on the south-eastern outskirts of London showed that influenza was diagnosed in 28% of 253 women of child-bearing age during the months of September and October, 1957. Accordingly 661 women attending the antenatal clinic at the Central Middlesex Hospital, London, between November, 1957, and March, 1958, were interviewed, and 240 (36·3%) said that they had had influenza since the summer of 1957. Subsequently 175 of these women were delivered of 177 infants in the hospital; 128 of them were accepted (on the criteria given) as having had influenza and 47 were not. Of the 50 infants born to women with medical confirmation of influenza, 2 showed abnormalities, but in these cases the influenza had preceded conception by 2 months in one and 2½ weeks in the other. Of 22 infants born to women who had had influenza in the first trimester of pregnancy, none had defects.

It is then pointed out that, taken at its worst, 63 of the "accepted" mothers had influenza during the first trimester, and 2 of their infants had defects: on the other hand, of 66 women with "accepted" influenza either before pregnancy or in the second or third trimester, 2 of their infants also had defects. An alternative comparison is between 2 defective children out of 89 born to mothers with influenza during pregnancy (2·2%), and 27 such children out of 1,996 live births in the same hospital during 1953 (1·35%). The authors conclude that there is no clear evidence from these data of congenital defects following Asian influenza in pregnancy, although a positive effect had been reported in earlier studies and an increase in the stillbirth rate due to anencephaly in Scotland in 1958 and to a lesser extent in 1959 has been recorded, suggesting that Asian influenza in the early months of pregnancy could increase the risks of anencephaly in an area where its incidence is normally high.

F. T. H. Wood

1087. **Long-term Follow-up of Hydrocephalic Infants Treated by Operation**

A. R. Taylor, J. R. Milliken, and P. P. Davison. *British Medical Journal* [*Brit. med. J.*] **2**, 1356–1359, Nov. 5, 1960. 2 figs., 9 refs.

In this paper from the Royal Victoria Hospital and the Child Guidance Clinic, Belfast, a follow-up study is reported of 8 infants who were operated on in 1952 for communicating hydrocephalus by the technique of thecoperitoneal shunt.

Of the 8 infants, 3 died within a year of operation; the remaining 5 have been followed up and their present condition has been assessed by a psychologist, a psychiatrist, and a neurosurgeon. The first child, a premature infant who is now 7½ years of age, has poor vision, nystagmus, and a squint, but otherwise is well and has an I.Q. of 100 (Stanford–Binet). [There is no mention of the skull circumference at this age.] The second child was 8 months old at operation and had a residual brain thickness of 0·5 cm. in the frontal lobe. He has residual spasticity of the legs, but his scholastic progress is average and his I.Q. is 104. The third infant, who was 10 months old at operation, did not walk until the age of 2 years 3 months; when 4 years of age she had two convulsions, but was said to be "82% normal". No formal I.Q. test was performed. From the latest report she appears to have no motor defects. The fourth infant was operated on at the age of 4 months. At 3 years 2 months he became ill, with vomiting, paralytic squint, papilloedema, and nystagmus. The head circumference then was 54 cm. (48 cm. at 4 months). A revision of the shunt resulted in improvement, but at the age of 6 years 8 months a similar episode of vomiting and drowsiness occurred; this time the shunt was replaced by a ventriculo-caval shunt (Spitz–Holter). When last seen at the age of 8 years the boy was well, with an I.Q. of 108. The 5th infant was operated on when 11 months old. At the age of 2½ years he appeared to develop a transverse myelitis with flaccid paraplegia, anaesthesia, and lack of sphincter control; later there was some recovery and his legs became spastic. At present he attends school and has an I.Q. of 110.

All 5 children had communicating congenital hydrocephalus unassociated with spina bifida cystica [and were thus in the most favourable group of patients]. The authors state that criteria for operation have not yet been established.

John Lorber

1088. **Amniocentesis in Haemolytic Disease of the Newborn**

W. Cary. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 778–781, Nov. 12, 1960. 5 figs., 4 refs.

Accurate antenatal prediction of the presence and severity of haemolytic disease of the newborn would greatly assist in the management of the individual case, and could at times be life-saving to the infant. Prediction based on the maternal antibody titre has not proved reliable in many centres, and alternative methods are still being sought.

One such method is to measure the bilirubin level in the amniotic fluid. If the optical density of the liquor amnii is plotted against the logarithmic scale of its wavelength the shape and the vertical height of the resultant curve will reflect the concentration of bilirubin and oxyhaemoglobin in the fluid. This observation, originally

made by Bevis (*J. Obstet. Gynaec. Brit. Emp.*, 1956, **63**, 68), has been utilized in the management of 40 pregnancies at the Royal Prince Albert Hospital, Sydney, with helpful results.

Amniocentesis, with local anaesthesia and a fine lumbar-puncture needle, was carried out 89 times on 40 patients, usually by the obstetric registrar and with no ill effects to any mother or baby. Of the 40 babies, 5 were Rh-negative; this was predicted 3 times but missed twice. One error might have been avoided had a second paracentesis been performed; in the other case the first sample was not obtained until the 37th week of pregnancy. In accordance with the results of the amniocentesis, labour was induced between 32 and 36 weeks in 16 cases; 2 of the babies died. In addition one hydropic baby was delivered spontaneously at 32 weeks and died and there was one other hydropic stillbirth, but here the exact duration of pregnancy was uncertain.

The author concludes that the test is relatively easy and accurate for the antenatal prediction of haemolytic disease, but stresses that paracentesis should first be performed at 30 weeks and repeated 2 weeks later. The relatively flat curve obtained when the baby is unaffected contrasts with the higher peaked curve when the disease is present. *F. P. Hudson*

1089. **Toxoplasmosis in Children: a Report of Twelve Cases**

M. W. Paterson. *Scottish Medical Journal* [*Scot. med. J.*] **5**, 467–476, Nov., 1960. 4 figs., 22 refs.

During the years 1948 to 1959 12 children were admitted to the Royal Hospital for Sick Children, Glasgow, in whom the diagnosis of toxoplasmosis was made on the basis of the clinical picture, radiography, and the results of serological tests. The signs and symptoms were in the majority of cases mainly referable to the visual apparatus and to the central nervous system, while 3 had purpura. Characteristic intracranial calcification was demonstrated radiographically in 50% of cases. The author divides the 12 cases into 2 groups, 11 suffering from congenital and one from acquired toxoplasmosis. The latter patient, aged 10 years, was admitted with lymphadenopathy. The age at admission of the other 11 patients was below 2 years. Details of the clinical and serological findings in each case are given and the treatment of the disease is briefly discussed, the administration of pyrimethamine and a sulphonamide being considered the most promising method. *Franz Heimann*

1090. **A Syndrome of Phenylketonuria with Normal Intelligence and Behavior Disturbances**

B. S. Sutherland, H. K. Berry, and H. C. Shirkey. *Journal of Pediatrics* [*J. Pediat.*] **57**, 521–525, Oct., 1960. 12 refs.

The discovery of the association of phenylketonuria with mental retardation represented a considerable advance in medical knowledge. Recently various authors have described patients with phenylketonuria but without mental retardation and in this paper from the University of Cincinnati, Ohio, 10 such cases are briefly summarized. To these the authors now add a further 2 cases. One patient, a boy aged 3½, was mentally normal (I.Q. 93) and the other, a girl aged 7, was slightly below normal (I.Q. 65). However, both children showed psychological disturbances manifested by a dull and expressionless facies, negative and apprehensive behaviour, emotional outbursts, and speech retardation. The boy was treated with a phenylalanine-restricted diet with resultant marked improvement in his behaviour. Although a similar diet prescribed for the girl was not maintained after her discharge from hospital, she appeared to become "livelier, more friendly, and co-operative". The serum phenylalanine level in both these children was considerably lower than that usually found in those who are mentally retarded. A study of the published cases referred to above also revealed that lower serum phenylalanine concentrations are often found in phenylketonuric patients with normal or near normal mentality.

David Morris

1091. **Cold Injury among Children Severely Ill in the Tropics**

D. C. Morley. *Lancet* [*Lancet*] **2**, 1170–1171, Nov. 26, 1960. 6 refs.

In a hospital in Nigeria 19 children were seen within 3 months with temperatures below 95° F. [35° C.]; 9 of these children died. The commonest clinical diagnosis was kwashiorkor, this being found in 8 of the 19 children. Separation from close contact with the mother is suggested as the principal reason for this condition arising in these sick children.—[Author's summary.]

1092. **Hiatal Hernias in Children: Special Reference to the Short Esophagus**

A. M. Olsen, C. B. Holman, and L. E. Harris. *Diseases of the Chest* [*Dis. Chest*] **38**, 495–506, Nov., 1960. 7 figs., 17 refs.

The authors report that 20 cases of hiatus hernia in children have been seen at the Mayo Clinic since 1950. The rarity of the condition may be judged from the fact that during the same period more than 17,000 cases of hiatus hernia in adults were diagnosed at the Clinic. All the children were under 14 years of age and "although most of them were seen early in life, some of them have been followed for as long as 20 years". The hernia was para-oesophageal in 2 cases and of the sliding type in one; the remaining 17 patients had a short oesophagus with intrathoracic stomach.

The 2 cases of para-oesophageal hernia both occurred in male infants, aged 1 week and 4 months respectively, who were admitted as emergencies with signs of gastrointestinal obstruction. In both cases the entire stomach had herniated through the hiatus and operation was immediately performed. The younger infant died, but the other is well and now aged 9 years. The child with the sliding hernia was seen at the age of 3 months and was treated conservatively in the first instance, but when 10 months old he developed severe ulcerative oesophagitis. The hernia was repaired by a transthoracic approach and the boy remains well 2½ years later.

In the other 17 children a short oesophagus was demonstrated by radiology or endoscopy. In one case,

in a girl aged 5 years, the diagnosis was made at routine investigation for congenital heart disease. As the patient was asymptomatic no treatment was considered, but she died following cardiac catheterization; necropsy revealed that this was probably a case of true congenital short oesophagus. In another patient, a boy aged 3 years, the condition followed the swallowing of lye and the development of severe oesophageal strictures. Conservative treatment by dilatation was performed at first, but ultimately a total oesophagectomy was performed with gastro-pharyngostomy. He survived the operation, but never made satisfactory progress and died aged 8 years. In a further 4 cases there had been dysphagia from birth. All had long strictures of the oesophagus with an intrathoracic stomach and it is suggested that these were all congenital in origin. Oesophagectomy was performed in one case, but the patient died following the operation. The other 3 were treated by repeated dilatation with satisfactory results; they have been followed up for 2, 11, and 3 years respectively. Of 9 cases which presented with a history of oesophageal regurgitation since birth and subsequently developed stricture and short oesophagus, 6 have been treated by dilatation with satisfactory results. A 7th patient underwent oesophagectomy and replacement with a section of colon with excellent results. The remaining 2, treated by dilatation initially, were lost to follow-up. The last 2 cases presented later in life with symptoms of oesophageal obstruction without a previous history of reflux. The first patient, a boy aged 7 years, was treated by dilatation only, while the second, a boy aged 14 years, was treated by vagotomy and pyloroplasty, followed by dilatation; both have made good progress. The authors state that no satisfactory explanation can be offered in these 2 cases, but as one had an oesophageal ulcer it is suggested that this was a Barrett ulcer and associated with a columnar-celled lining of the lower oesophagus.

In the authors' long discussion emphasis is placed on conservative treatment in cases of short oesophagus, this having proved satisfactory in two-thirds of their cases. On the other hand in cases of para-oesophageal and sliding hernia the possibility of operative repair must be considered. *Andrew M. Desmond*

1093. **Ulcerative Enterocolitis in Early Infancy (Report of Six Cases).** [In English]
M. Ergas. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **195**, 227–238, Oct., 1960. 29 refs.

Seven cases of ulcerative enterocolitis occurring in infants are reported from the " Assaf Harofe " Hospital, Tel-Aviv, Israel. All began to suffer symptoms in the first month of life, the clinical features consisting of progressive diarrhoea, distension and swelling of the abdomen, and ileus, followed in 6 of the 7 cases by death. Treatment was ineffectual. Necropsy revealed ulceration in both small and large bowels. The ulcers went through all the layers of the gut and were associated with a non-specific cellular infiltration. Although no proof was found, it was believed that the cause of this condition was infection with *Staphylococcus aureus*.
John Fry

1094. **Liver Function Tests in Infants with Biliary Atresia: Report of 30 Cases**
J. Kumate, F. Beltrán, L. Benavides, and M. A. Flores. *Pediatrics* [*Pediatrics*] **26**, 630–640, Oct., 1960. 7 figs., 27 refs.

Simultaneous changes of serum bilirubin (direct:total ratio), flocculation tests (thymol and cephalin-cholesterol), transaminases (GOT and GPT), serum cholinesterase and serial clearance of BSP [" bromsulphalein "] were studied in 30 cases of biliary atresia confirmed by exploratory laparotomy or necropsy.

Serum bilirubin generally showed a tendency to increase as age advanced (more evident after the fourth month) although its correlation was poor ($r=0{\cdot}31$). In over 80% of the cases, the direct:total ratio was 0·50 or greater. Flocculation tests showed abnormal values in over 35% of the cases and were more marked as age and degree of malnutrition increased. Transaminase activities in the serum showed slight increases (about 100 units/ml.), predominantly of GOT and without relation to age, nutritional condition or flocculation tests. Subnormal activity of cholinesterase was observed in three-fourths of the cases; it was more evident in older patients and no relation was found to percentage of the patient's theoretic weight. Serial study of BSP clearance showed increase of retention at 45 minutes (about 30%) and exponential elimination (with a half-life of 2·4 days) and levels above 6% by the fifth day following administration of the dye. —[Authors' summary.]

1095. **The Use of Cortisone in the Treatment of Severe Pneumonia in Children during the First Year of Life.** (Применение кортизона в комплексной терапии тяжелой пневмонии у детей первого года жизни)
R. A. Patušinskaja and E. V. Stroeva. *Педиатрия* [*Pediatrija*] **38**, 49–54, Nov., 1960. 10 refs.

Dyspnoea is usually the first symptom of pneumonia. The younger the child, the earlier appears the condition of respiratory-circulatory insufficiency and so more quickly may the child succumb. Antibiotics alone cannot help the child out of this respiratory dilemma. In such cases the authors recommend the use of cortisone, which has an anti-shock, anti-histamine, and anti-inflammatory action and also increases the antitoxic function of the liver.

In the present study cortisone was given to 31 children with pneumonia in addition to the usual supportive therapy, which included good nursing, adequate feeding, abundance of vitamins, especially vitamin D, oxygen therapy when required, a combination of two antibiotics, and cardiac stimulants if necessary. The initial dosage of cortisone was 5 mg. per kg. body weight given intramuscularly in 3 or 4 doses, this dose being reduced every 2 days during the period of administration, which lasted from 5 to 8 days. The total dose of cortisone, which varied according to the weight of the patient and the severity of the condition, ranged from 50 to 160 mg. In 22 cases cortisone was administered right from the start. In all cases amelioration of the respiratory and circulatory symptoms was observed within 12 to 24 hours (in a few cases within a few hours) and none of these patients

died. In the control group, which consisted of 18 children who were not given cortisone, 5 died.

H. W. Swann

1096. **Further Experience with Thiosemicarbazone in the Treatment of the Nephrotic Syndrome in Childhood.** (Weitere Erfahrungen mit der Thiosemicarbazontherapie beim nephrotischen Syndrom im Kindesalter)

H. W. RAUTENBURG. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **108**, 452–455, Oct., 1960. 20 refs.

The author reports his results in 20 children suffering from the nephrotic syndrome and 2 from recurrence of the syndrome who have been treated with thiosemicarbazone since 1951 at the University Paediatric Clinic, Berlin. His regimen is as follows. After the condition of the teeth and tonsils have been attended to all nephrotic children are given a salt-free, high-protein diet. Since thiosemicarbazone has been found to be especially effective in cases of nephrosis unresponsive to ACTH and the steroid hormones the author first observes the effect over 4 to 6 weeks of prednisone in daily doses of 1 mg. per kg. body weight before instituting treatment with thiosemicarbazone. The latter drug is administered in courses, of which the first lasts 5 days and subsequent courses 10 days, separated by treatment-free intervals of 3 or 4 days. The minimum duration of treatment, to be effective, is 10 courses given over 4 to 5 months, but the author favours 17 to 20 courses. During the first course the daily dosage of the drug is 0·25 to 0·5 mg. per kg. and this is then gradually increased in subsequent courses until a maximum of 2 to 5 mg. per kg. is reached. A too rapid increase in the dosage is the most probable aetiological factor in the production of hepatic toxicity, which is the most serious and unpredictable side-effect of this drug. Of the 22 cases, 15 were classified as " nephritic nephrosis ", that is, nephrosis with a history of antecedent renal inflammation, and the other 7 cases as " lipoid nephrosis ". In regard to course, 4 cases ran an acute course, in 5 the nephrosis was " dry ", with albuminuria and plasma changes, but without oedema, and in 13 phases of nephrosis alternated with periods of remission. The outcome was assessed as (1) completely recovered; (2) partially recovered, with residual albuminuria (from which some patients recovered completely); and (3) regression to chronic nephritis; (this last carried a poor prognosis because of the tendency to develop uraemia).

A good response to thiosemicarbazone was observed in 13 of the patients, of whom ultimately 7 recovered completely, 3 partially, and 3 developed chronic nephritis. A moderately good response was obtained in a further 3, but in 6 there was no response at all; it is pointed out that only 2 of these last 9 children were adequately treated, receiving 12 and 17 courses respectively, and their failure to respond remained unexplained. Of the 7 patients inadequately treated, one died during the 5th course from generalized oedema; in 2 cases initial treatment with steroids was contraindicated because of the presence of infection and thiosemicarbazone was administered only temporarily, while in 4 the drug had to be withdrawn because of hepatotoxicity. This condition occurred 6 times, but irreversible changes were not encountered and the symptoms disappeared within a short time of withdrawal of the drug; in one mild case therapy was continued with success on a reduced dosage. In the author's opinion thiosemicarbazone is a valuable agent in the treatment of the nephrotic syndrome in childhood. It probably has a direct action on the kidneys via the central nervous system and also an extrarenal action whereby it increases the steroid metabolism of the body and stimulates ACTH production.

E. S. Wyder

1097. **Nephritis Associated with Anaphylactoid Purpura in Childhood: Clinical Observations and Prognosis**

E. C. BURKE, S. D. MILLS, and G. B. STICKLER. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 641–648, Oct. 26 [received Dec.], 1960. 2 figs., 9 refs.

This paper reports the incidence of nephritis among 88 cases of anaphylactoid purpura occurring in children at the Mayo Clinic during the period 1935–58 and describes the results of follow-up observations. Of these children, 39 (44%) were considered to have had an associated nephritis. Although the age distribution of the whole series showed the incidence of anaphylactoid purpura to be highest at 2 to 4 years, the disease was more severe and more likely to be associated with nephritis at 5 years and over. Thus at 2 years only one patient out of 13 had nephritis, whereas at 5 years 8 out of 10 were affected.

Of the 39 patients with nephritis, 35 were followed up. Eleven were examined by the authors or reported on by their own physician less than 5 years after the initial illness; of these, 7 were healthy, 2 had persistent nephritis, and 2 had died from renal failure with hypertension. Of the 24 patients followed up 5 to 24 years after the illness, 21 were healthy, one had persistent nephritis, and 2 had died from renal failure. [The over-all survival rate was therefore 80%, and 71% were completely normal.] In contrast, of 35 patients who had anaphylactoid purpura without renal involvement, none subsequently developed nephritis and all were healthy at follow-up (in 9 cases less than 5 years and in 26 cases 5 to 24 years after the initial illness).

It is concluded that anaphylactoid purpura, even when associated with nephritis, has a more favourable prognosis than is generally supposed.

Hewett A. Ellis

1098. **Diagnosis of Acute and Chronic Pyelonephritis in Children: Use of a Simple Spread Plate Technique for Colony Counting**

N. H. HINKLE, J. C. PARTIN, and C. D. WEST. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 333–340, Sept., 1960. 2 figs., 14 refs.

The early diagnosis of the atypical case of acute pyelonephritis, which may present with only fever, is important if the patient is to escape permanent renal damage. The absence of pyuria in some cases showing bacteriuria has been frequently reported. The authors, writing from the University of Cincinnati College of Medicine, Ohio, consider that the clean-voided collection and quantitative

culture of urinary specimens provide the only reliable means of detecting insidious urinary-tract infection. The well-known method of obtaining clean-voided urine in both sexes is described at length; they state that the chance of introducing infection by a single catheterization has been estimated to be between 3 and 6%. Although the pour-plate method of culture with clean-voided urinary samples is satisfactory, it is only practicable in a well-equipped bacteriological laboratory, and an easier alternative is the spread-plate technique, which they claim gives a range of bacterial counts sufficient to exclude nearly all non-infected cases. In this method (using a dropper delivering 20 drops per ml.) 2 drops (0·1 ml.) of a clean-voided specimen of urine are allowed to fall on to the surface of a trypticase–soy–agar plate and are immediately spread over the entire plate with an L-shaped sterile glass rod; the plate is then incubated at 37° C. for 24 hours, at the end of which the colonies are counted as in the pour-plate method. "Ten times the number of colonies on the plate equals the number of bacteria per milliliter of urine." The method is simpler and just as reliable as the pour-plate method, although it has the theoretical disadvantage that the maximum accurate count possible by it is 3,000 colonies per ml., but in practice this level is sufficient to exclude all cases without infection. The authors conclude that a count of more than 10,000 organisms per ml. of urine is definitely diagnostic of urinary-tract infection.

J. M. Browne Kutschbach

1099. **The Prognosis of Subdural Effusions Complicating Pyogenic Meningitis**

P. Benson, W. L. Nyhan, and H. Shimizu. *Journal of Pediatrics* [*J. Pediat.*] **57**, 670–683, Nov., 1960. 26 refs.

The prognosis in cases of subdural effusion complicating pyogenic meningitis was studied at follow-up examination of all patients treated for acute purulent meningitis at the Harriet Lane Home, Baltimore, between 1949 and 1959. During that period subdural aspiration was carried out on 109 (34%) of 320 patients, effusions being found in 67. Most commonly the meningitis was due to infection with *Haemophilus influenzae* (47 patients) or *Pneumococcus* (25 patients). Subdural aspiration was performed as a routine on 50 patients, in half of whom an effusion was found; on other patients this procedure was carried out for recurrent and persistent pyrexia lasting over 48 hours, convulsions, or lethargy, coma, and irritability lasting over 48 hours. Aspiration was repeated on 45 patients until no fluid was obtained; trephination was performed on 11 and craniotomy on 11.

At follow-up examination, which in half the cases was more than 4 years after the onset of meningitis, the findings in the patients with an effusion were compared with those in patients from whom no fluid was obtained. There was no significant difference between the two groups in either mortality or the incidence of residual neurological sequelae, changes in the electroencephalogram (EEG), or hearing and speech defects. Sequelae were less commonly found if the interval between diagnosis and the start of treatment was less than 24 hours, if the volume of the effusion was less than 15 ml., and if coma and convulsions did not occur before treatment began. The long-term prognosis was better when membranes were excised; in 7 out of 8 patients from whom membranes were removed there were no sequelae, but in 5 of 7 from whom membranes were not removed clinical and neurological abnormalities were present and in one of the remaining 2 clinically normal patients the EEG was abnormal. Sequelae were also less frequent when aspiration was continued until no fluid was obtained than when only some of the fluid was removed.

The authors make a plea for aspiration as a routine, since the presence of effusion in one-third of their series was diagnosed by this procedure alone. *R. M. Todd*

1100. **Infantile Autism. An Analysis of 50 Cases and a Consideration of Certain Relevant Neurophysiologic Concepts.**

R. J. Schain and H. Yannet. *Journal of Pediatrics* [*J. Pediat.*] **57**, 560–567, Oct., 1960. 36 refs.

Since Kanner's original description (*J. Pediat.*, 1944, **25**, 211) of 11 children with "early infantile autism" there has been considerable controversy on the nomenclature and classification of the condition. In this paper from Yale University School of Medicine the clinical findings in 50 such children admitted to the Southbury Training School for mental defectives are described and discussed. The criteria for inclusion were a history of onset, during the first 2 years of life, of a personality disorder manifested by extreme self-preoccupation and unrelatedness to other persons in the environment and the absence of a history of serious motor retardation. The ages of the patients, 31 boys and 19 girls, ranged from 3 to 13 years and the duration of their stay in the school from 6 months to 10 years, mean 3·4 years.

Close scrutiny failed to reveal anything significant in the family history or in the patients' antenatal or perinatal history. All of them gave low psychometric test scores. Neurological examination revealed no abnormality in the central nervous system, nor was there any special history of past illnesses, but speech was grossly defective in all of them. The only important fact that emerged was a history of "seizures" in 21 cases, 10 of these patients having been diagnosed as epileptics on admission to the school; the seizures took the form of infantile spasms, grand mal, or psychomotor attacks. The incidence of at least one seizure in the group—42%—was significantly higher than in the average child population, which has been estimated to be about 7%. The laboratory data [unfortunately very inadequate] show that the radiographs of the skull (available in 8 cases) were normal, and in 3 cases air encephalograms obtained elsewhere had been reported as showing cerebral atrophy, but this is dismissed by the authors as "of questionable significance". Of the electroencephalograms obtained from 11 children, 6 were normal and 5 taken during a seizure showed diffusely abnormal tracings compatible with an epileptic disorder. On the basis of the relatively high incidence of seizures the authors speculate on the possibility of some lesion in the "limbic system" (roughly equivalent to the rhinencephalon) which might account for both the seizures and the severe disorder of affect. *David Morris*

Medical Genetics

1101. **Chromosome Translocation as a Cause of Familial Mongolism**
C. O. CARTER, J. L. HAMERTON, P. E. POLANI, A. GUNALP, and S. D. V. WELLER. *Lancet* [*Lancet*] **2**, 678–680, Sept. 24, 1960. 6 figs., 6 refs.

The hypothesis that chromosome translocation provides the mechanism by which some apparently normal parents have mongol children was tested in the case of a mongol child who had attended the Hospital for Sick Children, London, the chromosomal constitution of several of the child's relatives also being studied. The patient had 46 chromosomes, which included 2 representatives of chromosome 21 and an anomalous chromosome thought to be caused by a translocation between chromosomes 15 and 21. The patient's mother, maternal grandmother, and a maternal aunt each had 45 chromosomes, which included one chromosome 21 and also the 15/21 anomalous chromosome which occurred in the patient. The father and a brother of the patient each had 46 chromosomes which were apparently normal. Another brother and a cousin, who both died in infancy, had also been mongols. It appeared that the translocation 15/21 had occurred at least as early as the embryogenesis of the grandmother. *H. Harris*

1102. **Four Haemoglobins in One Individual: a Study of the Genetic Interaction of Hb-G and Hb-C**
A. B. RAPER, D. B. GAMMACK, E. R. HUEHNS, and E. M. SHOOTER. *British Medical Journal* [*Brit. med. J.*] **2**, 1257–1261, Oct. 29, 1960. 10 figs., 24 refs.

Human adult haemoglobin (Hb–A) consists of two pairs of polypeptide sub-units, that is, two α-chains and two β-chains, with a haem group attached to each chain, and its molecular formula may be written $\alpha_2\beta_2$ (or $\alpha_2{}^A\beta_2{}^A$). The abnormal haemoglobin C (Hb–C) differs from Hb–A in the amino-acid composition of the β-chains but not in the composition of the α-chains. Other abnormal haemoglobins have the same β-chains as Hb–A but differ in their α-chains. The present study from the Royal Infirmary, Bristol, and University College, London, is concerned with an individual who has inherited a haemoglobin with an abnormal α-chain (Hb–$G_{Bristol}$) from his mother and, presumably, Hb–C from his father. He therefore has the genes for 4 different types of sub-unit—normal α_2 and abnormal β_2 to form Hb–C, and abnormal α_2 and normal β_2 to form Hb–$G_{Bristol}$. The sub-units are formed independently and therefore the normal α_2 and β_2 sub-units combine to produce Hb–A and the abnormal $\alpha_2{}^G$ and $\beta_2{}^C$ combine to form a hybrid, Hb–$G_{Bristol}$/C. This hybridization *in vivo* has been confirmed by experiments *in vitro* in which Hb–$G_{Bristol}$ and Hb–C were added together and, by lowering the *p*H, dissociated into their four different types of sub-unit, $\alpha_2{}^G$, β_2, α_2, and $\beta_2{}^C$. The sub-units were then recombined by raising the *p*H and the recombination occurred at random, giving rise to 4 haemoglobins instead of the original 2. The independent inheritance of the α- and β-chains is also borne out by the fact that marriage of the propositus with a normal (Hb–A) woman resulted in 2 children with haemoglobins A+C and one with the same four haemoglobins as the propositus. This suggests that this third child inherited the abnormal α- and β-chains from its father and the normal sub-units from its mother. The results of this study support the idea that synthesis of adult haemoglobin is controlled by at least two pairs of genes. Furthermore, they suggest that each individual gene determines the synthesis of a particular type of sub-unit, and that these independently synthesized sub-units subsequently associate to produce the haemoglobins found in the erythrocytes. *H. Lehmann*

1103. **Progressive Muscular Dystrophy of the Duchenne Type in Females and Its Mode of Inheritance**
V. DUBOWITZ. *Brain* [*Brain*] **83**, 432–439, Sept., 1960. 17 refs.

There are at least two different modes of inheritance which can produce progressive muscular dystrophy of a similar pattern in childhood. While the majority of cases of severe classical Duchenne-type are due to a sex-linked recessive gene, some are due to an autosomal recessive gene. This accounts for the occurrence of the disease in females and is probably also responsible for some of the isolated cases in males. The more benign form of the disease, with a similar clinical pattern of muscular involvement to the Duchenne-type, may also be carried by either an autosomal recessive or a sex-linked recessive gene.

There is an overlap clinically between the severe and the mild forms in childhood, and there also appears to be a gradation from the mild form in childhood to that commencing in adolescence or adult life (including the limb-girdle type).

When the fundamental nature of muscular dystrophy becomes known it may well be found that these different genes all produce a similar basic biochemical or enzymatic defect but with a slight variation in its mode or degree of expression.—[Author's conclusions.]

1104. **Heredity in Gastroenterology: a Review**
R. B. MCCONNELL. *Gut* [*Gut*] **1**, 273–284, Dec., 1960. Bibliography.

1105. **Terminology in Genetic Syndromes.** [In English] J. BAUER. *Acta genetics medicae et gemellogiae* [*Acta Genet. med.* (*Roma*)] **10**, 63–69, Jan. [received March], 1961. 23 refs.

Public Health and Industrial Medicine

1106. **Effect of Smoking on General Health.** (Курение и здоровье (Опыт анкетного опроса населения))
S. M. Slinin. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **38**, 105–109, Oct., 1960.

The author reports that the analysis of the answers to an appropriate questionary addressed to 920 male smokers and 940 non-smokers revealed that general morbidity was about 3 to 4 times higher in smokers than in non-smokers. The increase was particularly pronounced in regard to diseases of the stomach, heart, and lungs. It was noted that morbidity decreased in persons who had given up smoking, and 93% of these reported noticing a general improvement in their health. No less than 79% of the smokers stated that they would have liked to give up smoking because they realized its adverse affect on their health, but had not sufficient will-power to do so.

The author recommends the establishment of special clinics where smokers, particularly those whose health is affected by the habit and those for whom smoking is absolutely contraindicated, could receive treatment to help them break the habit. *A. Orley*

1107. **A Study of Six Young Mentally Handicapped Children and Their Families**
J. Leeson. *Medical Officer* [*Med. Offr*] **104**, 311–314, Nov. 18, 1960. 4 refs.

This paper from the University of Manchester describes a detailed investigation of the problems encountered by the families of 6 severely mentally handicapped children aged 2 to 3½ years. The information was obtained in unprepared interviews with both parents. Brief reports of each case are given.

Because of their retarded development these children were as dependent as infants, yet they were more active, and in this lay the chief problem. In addition, 5 were incontinent and all had some physical disability, petit mal, or disturbed behaviour. The success of the family in meeting these problems and caring for the children within the community was dependent on the mother's good health, the material well-being of the family (good housing in particular), above-average domestic help from the father, and support from relatives.

At the time of the investigation it was felt that the available community services were inadequate. The parents appreciated the medical services where the doctor had taken them into his confidence early, with obvious sympathetic interest, and had given them the opportunity to discuss the problem on several occasions. Suggestions for facilitating the community care of these severely handicapped children include the following: (1) Daily training for children aged 2 and over in centres with staff trained to develop skills in handling this type of child, making use of full psychological assessment to cater for the child's individual needs. Transport should be provided to and from the centre. (2) In rehousing care should be taken to keep the family within reach of helpful relatives. (3) Facilities should be available for full and co-ordinated psychological, psychiatric, medical, and social assessment of the child, so that an integrated plan can be made for child and family; this should include counselling and support for the parents and facilities for meeting other parents with similar problems. Given this support, the families appear to be able to provide adequate care for severely subnormal children, who are accepted tolerantly by their siblings (who do not appear to suffer any obvious psychological trauma) and by the community. *Christopher Wardle*

1108. **Juvenile Delinquency.** (Die Jugendkriminalität)
P. Schumm. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortsch. Neurol. Psychiat.*] **28**, 521–555, Oct., 1960. 2 figs., bibliography.

This paper surveys critically the considerable German literature on the subject of juvenile delinquency from 1956 to 1959. It gives the more important statistics and describes work on conditions and causal factors, including sociological as well as psychodynamic theories. Riots, vandalism, traffic offences, and sexual delinquency are discussed, together with the corresponding legal provisions such as juvenile courts and their procedure. Finally, reports and articles dealing with children and young persons as witnesses in court and as victims of assaults are surveyed and discussed.
W. Mayer-Gross

1109. **Salmonellosis Spread by a Dietary Supplement of Avian Source**
F. R. Philbrook, R. A. MacCready, H. Van Roekel, E. S. Anderson, C. F. Smyser Jr., F. J. Sanen, and W. M. Groton. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 713–718, Oct. 13, 1960. 13 refs.

An outbreak of salmonellosis due to *Salmonella typhimurium* in a Massachusetts mental hospital is described. Among 1,850 inmates there were 104 cases of the disease, with 4 deaths directly attributable to it and 2 in which salmonellosis was regarded as a contributing factor.

Some of the epidemiological problems are described. The source of the infection was traced eventually to a dietary supplement, eggnog (made from raw eggs, pasteurized milk, vanilla, and sugar). None of the persons concerned in preparing the eggnog was infected, but a retrospective analysis of three previous outbreaks also appeared to incriminate eggnog and suspicion consequently fell on the eggs themselves, which came from a nearby farm colony. A serological and bacteriological investigation of fowls and eggs at this colony showed that infection was generalized in the birds. This part of the investigation was not undertaken until several

months after the epidemic, but phage typing gave strong corroborative evidence, cultures of *Salm. typhimurium* isolated from ovaries and eggs being of the same type (Type 1 var. 5) as two strains isolated from patients.

Reports of other outbreaks of salmonellosis due to infected eggs and egg products are discussed and a word of warning is given that a source of infection may be missed if the sample tested is too small. In the present investigation only 3 out of 1,117 eggs from 29 positively reacting birds were positive. The small proportion of eggs infected accounts for the occurrence of occasional sharp outbreaks rather than an endemic type of infection. It is urged that eggnog, a dietary supplement frequently used in mental institutions in the U.S.A., should not be served unless pasteurized. *Kurt Schwarz*

INDUSTRIAL MEDICINE

1110. **The Classification of Chest Radiographs for Coalworkers' Pneumoconiosis: a Study of the Performance of Two Readers over a Period of Six Years**
J. R. ASHFORD. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 293–303, Oct., 1960. 1 fig., 5 refs.

Two observers have been responsible for the classification of chest radiographs taken in the course of the National Coal Board's field research scheme which is being carried out at 25 British collieries. The films have been classified according to the International Labour Office Classification of 1953. Three different methods of reading have been employed by which both observers have read all the films once or twice and a " definitive " classification has been decided by joint consultation on films where the individual classifications have differed. It is thus possible to study both intra- and inter-observer variation of classification. At 5 collieries a second survey has been conducted after an interval of 2 years. Here a one-in-ten random sample of the radiographs from the first survey has been reclassified in the course of the second classification, thus providing a check on the consistency of classification over a period of time.

The proportion of consistent readings by either or both observers decreased almost linearly with the proportion of films showing pneumoconiosis, for it is only in those films in which pneumoconiosis is suspected that disagreement can arise. Both observers tended to show a bias of their readings in relation to the definitive readings, and this bias varied from positive to negative during the period covered by the surveys. The definitive readings showed a very small variation with time, except at one colliery where one observer had a temporary variation in his reading level. In this case a reclassification of the films was arranged. There was almost 100% consistency in classification of films where the original readings of the 2 observers agreed. In those in which there had been disagreement the consistency of the definitive readings varied from 54% to 76%.

It is concluded that the procedure adopted to obtain definitive readings leads to a reasonably stable reading standard and provides a satisfactory way of measuring the prevalence of radiological pneumoconiosis. But the presence of the systematic variations in individual reading level suggests that it would be desirable, in this sort of research, to increase the number of film readers. In this way any " averaging " procedure used to obtain definitive readings would provide more stable results than can be obtained with 2 readers. The procedure also enabled individual film readers to be made aware of fluctuations in their reading level and thus to be able to correct their standards. This close monitoring of standards has already led to an increase in the consistency of the routine readings by each individual, and has reduced the periodic fluctuations of the doctors' average standards of classification. *C. M. Fletcher*

1111. **The Relation between Lung Dust and Lung Pathology in Pneumoconiosis**
G. NAGELSCHMIDT. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 247–259, Oct., 1960. 3 figs., bibliography.

This paper reviews the technique of, and conclusions that may be reached from, comparing analyses of the quantity of dust and the pathological changes in the lungs in cases of pneumoconiosis. First, problems of sampling the lungs are discussed, and it is concluded that at least one-third, and preferably one-half, of the material from a pair of lungs should be available for analysis if the total amount of dust in them is to be determined. Separate analysis of peribronchial and hilar lymph nodes may provide additional information. A variety of methods are available for isolating the dust from the lungs; an example is given in which dusts isolated by 2 different methods in different laboratories were compared and very similar results obtained. Again, many physical and chemical methods are available for analysis of the composition of the dust. Lastly, the results may be expressed in various ways, none of which is entirely free from objections, but it is concluded that the least objectionable method is to express the result as a percentage of dried lung.

The author proceeds to review the results obtained in different forms of pneumoconiosis. In classic (hyaline nodular) silicosis 1 to 3 g. of quartz and 4 to 10 g. of total dust are found in the lungs with increasing degrees of fibrosis. The proportion of quartz in the dust ranges from 20% upwards. In pneumoconiosis of coal workers with massive fibrosis there is usually 40 to 50 g. of dust, over 80% of which is coal; the quartz content is of the order of 2 to 3%. Total dust averages 15% of the dried lung weight. In pneumoconiosis due to dusts free from quartz still higher quantities of dust are found; 90 g. of carbon has been found in both lungs in one case of pneumoconiosis in a carbon-electrode maker. Intermediate values have been found in lungs of haematite workers and foundry workers. The pathology in these cases is also intermediate between that of classic silicosis and pneumoconiosis due to dusts of low quartz content.

In the pneumoconioses that may be described as characterized by diffuse interstitial fibrosis (berylliosis,

aluminosis, and asbestosis) the dust content is extremely small.

In the discussion of these results it is suggested that in the latter form of fibrosis the dust may be partly soluble and may be removed from the lung during life. In this case it would be expected that the quantity of dust would diminish as the period since removal from exposure increases. There is some evidence that this may occur in asbestosis. In the case of insoluble dusts a distinction may be drawn between cases with a high proportion of quartz and those with a lower proportion. When this proportion is above 18% the pathology is usually characteristic of classic silicosis; when it is less the pathology tends to approach that of simple pneumoconiosis of coal workers. Finally there is a suggestion that in mixed soluble and insoluble dusts, as may occur in diatomite pneumoconiosis, there is a combination of interstitial and nodular fibrosis. It is possible that amorphous silica causes the interstitial and quartz and cristobalite the nodular fibrosis in these lungs. *C. M. Fletcher*

1112. **Lung Cancer Mortality Experience of Men in Certain Occupations in California**

J. E. Dunn Jr., G. Linden, and L. Breslow. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **50**, 1475–1487, Oct., 1960. 10 refs.

Occupational histories obtained from patients with and without lung cancer suggested that there might be a high risk of the disease in certain occupations in California. This possibility has now been investigated by the Bureau of Chronic Diseases of the State Department of Public Health, Berkeley, by observing the mortality from lung cancer among selected groups of men in different occupations over a period of years. Questionaries were sent to men in 10 selected occupations asking about the nature of their occupation and their smoking habits. Replies were received from nearly 67,000 men—85% of those written to. The mortality from lung cancer and from all other forms of cancer among these men over the next 3 to 4 years was obtained by matching the names of the men against the names of persons dying of cancer in California. Cases will have been missed if the men left the State and died elsewhere, but losses due to this cause are unlikely to have been more than 2% per year. The expected mortality from cancer was calculated from the age-specific death rates recorded in California at about the time of the 1950 census. In the case of lung cancer the expected mortality was obtained after multiplying by a factor to allow for the increase in mortality between 1950 and 1956; this factor was obtained by assuming that the rate of increase of mortality from cancer of the lung in California was the same as that in the U.S.A. as a whole.

The mortality from cancer other than that of the lung in the different occupational groups ranged from 67% to 133% of the expected mortality, and for the whole population studied was 85% of the expected figure. The mortality from lung cancer was 113% of the expected value and ranged from 26% in printers (2 cases observed) to 145% in painters (35 observed). The mortality from lung cancer in a control group of public utility employees was 86% of the expected (17 cases). Some of the excess mortality could be attributed to heavy cigarette smoking. Thus in the whole group the mortality was 29 times as high among men smoking 2 packets of cigarettes a day as among non-smokers. After allowing for variations in cigarette consumption and for an estimated number of missed cases it was calculated that lung cancer mortality was less than that expected among printers and sheet metal workers, equal to that expected in the control group, slightly above that expected among welders, plumbers, and marine engineers, and between 40 and 70% above that expected among asbestos workers, painters, and cooks. In the last two groups the excess was statistically significant.

It is pointed out that it is difficult to recognize an occupational risk of cancer of the lung, unless it is very large, because of the high risk from cigarette smoking. Doubling the risk among non-smokers in a particular occupation would lead to a total increase of only 14% among all male employees. *Richard Doll*

1113. **Fatal Gassing in an Acetylene Manufacturing Plant**

A. T. Jones. *Archives of Environmental Health* [*Arch. environm. Hlth*] **1**, 417–422, Nov., 1960. 3 figs., 4 refs.

In March, 1959, at an acetylene manufacturing plant in New South Wales, Australia, a man aged 24 was found dead with his head in the calcium carbide hopper. The principal findings at necropsy were singeing of the hair and eyebrows, oedema and redness of the air passages, congestion of the lungs, and 8% carboxyhaemoglobin in the blood.

The production process at the plant is fully described. Briefly, calcium carbide is fed into hoppers from which it passes automatically into gas-generating chambers. The hoppers are normally closed by a lid, which is removed at intervals to see whether more calcium carbide should be added. The atmosphere within the hoppers may be grossly deficient in oxygen and contain up to 80% of acetylene. It was thought that the man met his death from anoxia when carrying out this inspection.

W. K. S. Moore

1114. **Occupational Poisoning among Well-sinkers.** (Les intoxications des puisatiers)

V. Raymond. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **21**, 517–523, Sept. [received Nov.], 1960.

Intoxication due to exposure to gases in the soil, motor engine exhaust gases, and explosive gases account for about half the total accidents to men employed in sinking wells, the last two arising from modern methods used in the process. Soil gases, when heavy, may accumulate in the well and drive out the air or may contain volatile toxic vapours. These vapours, especially in volcanic soils or those containing lignite, consist chiefly of carbon dioxide, a product of spontaneous combustion or arising from the decomposition of organic matter. This gas displaces oxygen, causing accidents due to anoxia with sudden onset of syncope which, though of short duration, may cause the worker to release his hold on the cable and

fall to the bottom of the well. Pockets of sulphuretted hydrogen may also be present.

In this paper 3 fatal cases of CO_2 poisoning are described in detail; one man died from suffocation, one from cranial fracture, and one recovered after oxygen therapy. In a 4th case, in which the victim also died from fracture of the skull, hydrogen sulphide was demonstrated in the atmosphere in a concentration of at least 136 mg. per c. metre. In another series exhaust gases arising from the use of motor pumps were responsible for 8 cases of poisoning, 4 of them fatal. The gases incriminated were carbon monoxide and dioxide, sulphur dioxide, nitrated compounds, hydrocarbons, and other products of combustion. Explosives such as dynamite and " nitromit " give rise to carbon monoxide and nitrous compounds. Of 3 fatal cases described, one occurred in a mason with no previous experience of well-sinking or of explosives.

Among the preventive measures recommended are the provision of exhaust pipes leading to the upper air when petrol motors are used; tests of the atmospheric content of the well by modern techniques—the old test by means of a lighted candle is quite inadequate; purification of the atmosphere by aspiration or injection of pure air; roping of the workmen and provision for bringing them up in case of accident, together with facilities for immediate treatment by artificial respiration. In addition workmen should receive special training in modern techniques of well-sinking. *Ethel Browning*

1115. **The Effect of Prophylaxis with Calciumedetate in Workers Exposed to Lead.** (Effetti della profilassi con versenato di calcio negli operai esposti al piombo)
O. Bartolozzi and N. Zurlo. *Medicina del lavoro* [*Med. d. Lavoro*] **51**, 607–611, Oct. [received Dec.], 1960.

Writing from the University of Milan the authors describe the preventive measures in force at a factory in Milan making electric batteries. Although the factory is not a very modern one everything that can reasonably be asked for in the prevention of lead poisoning has been provided, including double rations of food in the factory canteen. In addition all operatives are medically inspected four times a year, when the blood is examined for signs of stippling; the haemoglobin value is determined twice a year, the urinary coproporphyrin content estimated once or twice a year as necessary, and if required workers are sent to the Clinic of Industrial Medicine for estimation of blood lead and protoporphyrin levels and urinary lead excretion. Also in the past 5 years 3 chest radiographs for each employee have been obtained.

In spite of these precautions the risk of lead poisoning still remains a threat. The authors therefore determined to try the effect of sodium calciumedetate (Ca EDTA) as an additional prophylactic measure. This substance was given to all employees in the factory each morning in the following dosage: 2 g. daily by mouth for 10 days, followed after 10 days' interval by another similar 10-day course. In some cases this cycle of treatment was repeated. In addition, vitamin B_{12}, liver extract, and iron were given. Apart from some slight initial intestinal disturbance in a few cases the drug was well tolerated and no side-effects were noted. Since this procedure was instituted the number of cases of frank lead poisoning has fallen from 9 in the period 1950–5 to 1 in the period 1955–9. Full details are presented in tables of the results of laboratory tests on some of the workers who had undergone 3 or 4 cycles of prophylactic treatment with Ca EDTA.

The authors conclude that the additional use of this chelating agent has proved an undoubted success and has given rise to no inconvenience. They stress, however, the following points. (1) Since the urinary coproporphyrin content fell and remained within normal limits for one year after treatment with Ca EDTA the determination of this factor is thus of no value as a periodic test. (2) The absence of any signs of lead poisoning even in workers with a high urinary lead content is worthy of note. (3) The difference between the daily amount of lead excreted in the urine and the amount absorbed daily suggests that there is a change in the renal threshold for lead; this finding, it is suggested, opens the way for new experiments on the capacity and limitations of this chelating agent. *W. K. Dunscombe*

1116. **Treatment of Severe Parathion Poisoning with 2-Pyridine Aldoxine Methiodide (2-PAM): Report of a Case**
A. J. Funckes. *Archives of Environmental Health* [*Arch. environm. Hlth*] **1**, 404–406, Nov., 1960. 9 refs.

An account is given of a case of poisoning by parathion successfully treated with 2-PAM (2-pyridine aldoxine methiodide). A 29-year-old white man, known to be careless in his habits, became dizzy and nauseated immediately after loading 2% parathion dust for 4 hours. He was found in a collapsed state half an hour later and given atropine, 1/50 grain (1·2 mg.) orally. An hour after exposure he had pin-point pupils and hyperidrosis. More atropine (1/75 gr. or 0·8 mg.) was given. Three hours later he was admitted to hospital and was given a warm bath and 1/30 gr. (2 mg.) of atropine intramuscularly. His condition continued to deteriorate, and moist breath sounds, clonic movements, and incontinence were added to the earlier signs. His blood pressure was 220/110 mm. Hg and his pulse rate 140 per minute and irregular. A further 1/30 gr. (2 mg.) of atropine was given intravenously.

An intravenous infusion of 1 g. of 2-PAM in 500 ml. of 0·2% saline was given 5¼ hours after the illness began, and was completed in 35 minutes. Improvement was observed within 10 minutes of starting the infusion; the patient became rational and convulsive movement ceased. Bladder control was achieved within 8 hours. Atropine was continued in decreasing dosage for 2 days.

The severity of the poisoning was indicated by the symptoms and the high level of *p*-nitrophenol excreted in the urine (108 μg. per hour) on the day after the patient was admitted to hospital. Erythrocyte and plasma cholinesterase estimations were unusual in that the erythrocyte level was higher than would be expected with the degree of illness and also by comparison with the lower level in the plasma. *W. K. S. Moore*

Forensic Medicine and Toxicology

1117. **Myelopolyneuritis Due to Tricresylphosphate. Mass Poisoning in Morocco in 1959.** (L'intoxication marocaine de 1959: myélopolynévrites tricrésylphosphatées)
H. Geoffroy, P. Pascal, A. Slomic, and M. Benebadji. *Presse médicale* [*Presse méd.*] **68**, 1474–1476, Sept. 17, 1960. 24 refs.

This paper gives an account of the outbreak in Morocco in 1959 of myelopolyneuritis due to mass poisoning with tri*ortho*cresylphosphate (TOCP). The origin of the poisoning was traced to criminal adulteration of edible oil with a rinsing oil used for aeroplane engines which contained TOCP; over 10,000 people were involved, all but one being Moroccan. The authors present a concise review of previous large-scale intoxications by TOCP, of which the first occurred in the U.S.A. during the period of prohibition, and then describe the clinical evolution of the intoxication, the laboratory and electrophysiological findings, and the various attempts at therapy. The initial pre-paralytic phase was initiated by a latent period lasting 8 to 35 days, sometimes with gastro-intestinal upsets immediately following the ingestion of the contaminated oil. After this some patients showed a prodromal catarrhal phase with slight fever. Paralysis was preceded by various subjective sensory disturbances and usually started in the great toe, spreading in the ensuing hours to the muscles of the foot and leg. About 10 days later the hands and arms were affected to a variable extent, the attack being essentially peripheral. Only rarely was the onset acute, but in these cases severe paralysis occurred within a few hours. After 4 weeks the peripheral flaccid paralysis seemed to become stationary, with absence of tendon reflexes in the regions involved.

The main and also a new clinical observation in this series was the finding of objective sensory disturbances in 20% of the cases; most previous authors have considered lesions due to this cause essentially motor. All subjects showed vasomotor disturbances, such as cyanosis and coldness in the limbs, but these were independent of the sensory changes. Sphincter involvement was rarer than expected, no meningeal signs were observed, and the results of various laboratory tests were negative. A mean diminution of some 25% in cholinesterase activity in the serum (Vincent's method) was observed, and the level did not return to normal for 4 months. Between the first and 9th months after the onset there was rapid regression of the initial sensory disturbances, a tendency to recovery of the peripheral flaccid paralysis after a stationary phase, some evidence of pyramidal tract involvement, and an excellent prognosis as to survival. The individual prognosis was related to the extent of involvement of the spinal cord.

Most of the patients were treated with vitamins B_1 (aneurine) and B_{12} and the authors consider, after comparison with the results in previous outbreaks, that these may have been of real value; the evolution of the intoxication was more rapid and more severe in patients given vitamin C alone than in those given vitamins B_1 and B_{12}. Pyridoxine and α-tocopherol were without effect. Among the alkaloids neither acetylcholine nor atropine was used, while physostigmine (eserine), neostigmine, and pyridostigmine proved ineffective. Pilocarpine, which was first used to investigate disorders of sweating, was found to produce some subjective as well as some clinical and biochemical improvement which could not be attributed solely to the vasomotor effect of the drug.

The authors conclude that spontaneous recovery from flaccid paralysis can be hastened by physiotherapy, but that the future is much darker for those patients with extensive involvement of the cord. *P. N. Magee*

1118. **Mass Intoxication by Oil Containing Cresyl Phosphates.** (Intoxication collective par une huile à base de crésylphosphates)
National Institute of Hygiene of Morocco. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2807–2840, Nov. 12, 1960. 5 figs., bibliography.

1119. **Salicylate—a Dangerous Drug in Infancy and Childhood: a Survey of 58 Cases of Salicylate Poisoning**
J. U. Crichton and G. B. Elliott. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 1144–1147, Nov. 26, 1960. 11 refs.

The authors report that the 58 cases of salicylate poisoning admitted to Calgary General Hospital, Canada, in the 4½ years ending in June, 1960, could be divided into three groups as follows: (1) 17 cases of attempted suicide in patients aged from 14 to over 60 years; (2) 27 cases of accidental ingestion of salicylate, all in children under 7 years of age; and (3) 14 cases due to the therapeutic administration of too large doses of the drug, also all in children under 7 years of age. In this paper they are concerned only with the contrast in the clinical picture presented by the patients in Groups 2 and 3, and the cases in Group 1 are not further considered.

The cardinal signs and symptoms of salicylate poisoning are hyperpnoea, dehydration, pyrexia, twitching or fits, haematemesis, and melaena. All but 2 of the children in Group 2 were sent to hospital with a diagnosis of overdose of salicylate. Of the 19 treated by gastric lavage, only one later developed hyperpnoea. One child on admission had abdominal pain, vomited blood, and later had some melaena and difficulty in breathing, but recovered, while another, the only patient in this group who died, was admitted with signs indicative of meningism, that is, stiffness of the neck and arching of the back. It was ascertained that 7 of these children had taken tablets of aspirin intended for adults, containing 5 grains

(325 mg.) of sodium salicylate, but the precise number of tablets was not known. It is stressed that in cases of salicylate poisoning, whether accidental or suicidal, gastric lavage is always worth while, for it has been shown that salicylate may remain in the stomach unabsorbed for many hours. Once absorbed, some 80% is excreted in the alkaline urine within 24 hours if sufficient base is available.

In the cases in Group 3 salicylism had not been considered in the clinical diagnosis before admission, although in each case some of the signs and symptoms were present. These 14 children had been treated with salicylates for such ailments as chickenpox, measles, head cold, upper respiratory infection, enteritis, or influenza. The toxic effects of salicylate, which brought them into hospital, had been diagnosed as pneumonia or variously pneumonia with coma, dehydration, and haematemesis. The commonest pitfall was the diagnosis of bronchopneumonia on account of the hyperpnoea (panting), pyrexia, and leucocytosis—the absence of sweating being overlooked. The uniform nature of the leucocytosis, which involved all types of leucocyte (counts up to 30,000 per c.mm.) typical of dehydration had not been distinguished from the polymorphonuclear leucocytosis to be expected in pneumonia. The chest radiograph of a dyspnoeic infant may be difficult to read, and an exposure made during expiration could have been misinterpreted as a lobar consolidation. In hospital analysis of the urine gave a positive reaction for salicylate or a strongly positive reaction for ketone bodies; no reducing substances were found. The level of salicylate in the blood, estimated in 7 cases, varied between 31 and 60 mg. per 100 ml. There is, however, no essential correlation between the blood salicylate level and the toxic symptoms. Moreover, the margins between the therapeutically effective salicylate serum level (30 to 35 mg. per 100 ml.), the toxic level (40 mg. per 100 ml.), and the minimum lethal level (50 mg. per 100 ml.) are narrow. The quantity ingested was stated in 6 cases only and varied from 15 grains (1 g.) in 24 hours to 100 grains (6·5 g.) in 5 days. There was marked depletion of the sodium and potassium ions in the blood, the serum potassium level falling in one case to 2·8 mEq. per litre. In this group 2 children died shortly after admission, both having severe dyspnoea, haematemesis, and melaena. They had been given adult-strength tablets of aspirin in the belief that the drug was harmless.

In discussion it is strongly urged that the public be informed that doses of salicylate suitable for adults are potentially fatal for young children; that such preparations should be labelled: " Not for a child under 5 years of age "; and that the toxicity of salicylates should be stressed in the training of medical students and nurses. The difficulty in the diagnosis of therapeutic intoxication is due to a number of factors, notably the obscure or concealed history, the coincidental illness, the repeated small doses given, the lapse of several days between the first dose and the appearance of symptoms, the serious condition of the child admitted with pyrexia, dehydration, and hyperpnoea, and lastly the delay in response to treatment, since gastric lavage is too seldom undertaken immediately.

The authors emphasize that signs of air hunger in a young infant should immediately direct suspicion to salicylate poisoning. *M. A. Dobbin Crawford*

1120. **Granulocytopenia Due to Chlorpromazine: a Report of 11 Cases**

S. C. CARFAGNO and J. T. MAGEE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **241**, 44–54, Jan., 1961. 39 refs.

1121. **Isolated Myocarditis as a Cause of Sudden Obscure Death**

C. CORBY. *Medicine, Science and the Law* [*Med. Sci. Law*] **1**, 23–31, Oct., 1960. 1 fig., 19 refs.

The author presents 32 cases of unexpected death in which macroscopic pathological changes were minimal or absent at necropsy and which on subsequent histological examination proved to be examples of " isolated myocarditis ". This is defined as " myocarditis of at present unknown aetiology, occurring without endocarditis or pericarditis and without any pathological process to account for the myocardial inflammation ". The youngest patient in the series was 5 years old, the eldest 50, and 17 were between 20 and 40 years old. The sex incidence was equal. In 28 of the cases the condition presented as a sudden catastrophe, the clinical picture frequently mimicking that of myocardial infarction; in the remaining 4 there was unexplained progressive heart failure. The previous medical history was of no significance and there was no evidence of drug-taking or allergy in any case. Toxicological investigations in 12 cases and virological studies in one gave negative results.

In every instance multiple sections from different areas of heart muscle revealed a patchy inflammation. The most characteristic histological feature was a degenerative change in the myocardial fibres varying from granular swelling with loss of cross-striation to complete muscular necrosis and replacement fibrosis. These degenerative changes were accompanied by an inflammatory infiltration of the area by a variety of cells, usually predominantly lymphocytes and monocytes. In two cases giant cells were predominant. The histological picture, however, is stated to vary widely from case to case and indeed from area to area of myocardium in the same case. Thus both interstitial and granulomatous inflammation may occur in the same heart, and the author adheres to the view that these are merely variations of the same basic disease process. In general in this series the lesions were most conspicuous in those patients with a prolonged symptomatology, and it is suggested that the duration of survival may depend upon the degree of involvement of the conducting system.

The aetiology is briefly discussed; it is admitted that the lesions are histologically indistinguishable from those found in myocarditis secondary to many known causes and the suggestion made that they represent a non-specific myocardial reaction to noxious stimuli of varying kind.

A plea is made for virus studies to be carried out in cases of this type. *Gilbert Forbes*

Anaesthetics

1122. **The Biological Role of Carbon Dioxide**
D. R. GODDARD. *Anesthesiology* [*Anesthesiology*] **21**, 587–596, Nov.–Dec., 1960. 34 refs.

In this study, reported from the University of Pennsylvania, Philadelphia, of the biological role of carbon dioxide (CO_2) it is pointed out that although life may have first evolved in a world of methane and organic compounds, all cellular and multicellular organisms require the gas and have done so for a long period of geological time. At one time it was thought that the only metabolic role of CO_2 was its utilization by green plants. Work done since 1940 with carbon isotopes has shown that the reactions of CO_2 release are reversible, contrary to previously held views. Carbon is the sixth most abundant element on earth, and by far the greater part of it is in the carbonate of rocks. The sea contains 55 times as much CO_2 as the atmosphere. The normal percentage of CO_2 in the air (0·03) can vary considerably as a result of industrial and biological activity. The author states that " an Iowa cornfield may remove 200 lb. of CO_2 per acre [36·3 kg. per hectare] per day " by photosynthesis.

W. Stanley Sykes

1123. **Elimination of Carbon Dioxide by the Lung**
J. F. NUNN. *Anesthesiology* [*Anesthesiology*] **21**, 620–633, Nov.–Dec., 1960. 7 figs., bibliography.

By far the greater part of the carbon dioxide (CO_2) eliminated from the body is removed by the lungs. The airflow here is tidal rather than fluvial; this tidal flow has two disadvantages—counter current flow is impossible and a proportion of each breath is wasted by the dead space of the air passages. During anaesthesia the patient often inhales CO_2 of endogenous or exogenous origin; moreover, the body has a large storage capacity for CO_2. Both these factors cause the elimination rate of CO_2 to differ from the production rate of the gas. Tracheal intubation reduces the dead space by about one-half. It is pointed out that there is also an alveolar dead space in emphysema.

W. Stanley Sykes

1124. **Acclimatization to Carbon Dioxide**
R. H. KELLOGG. *Anesthesiology* [*Anesthesiology*] **21**, 634–641, Nov.–Dec., 1960. 1 fig., 41 refs.

Certain aspects of acclimatization to carbon dioxide (CO_2) have been studied at the University of California School of Medicine, San Francisco. It is pointed out that the alveolar tension of CO_2 normally remains very constant at about 40 mm. Hg over a fairly wide range of altitudes—from a deep mine to about 1,350 metres. However, several millions of people live at such altitudes that 33 mm. or even 29 mm. Hg is not abnormal for them. Adaptation begins in a few hours and takes from 2 to 5 days to reach a steady level. On descent from high altitudes the reverse shift of the CO_2 response curve takes up to a month to achieve the original level.

W. Stanley Sykes

1125. **The Use of Hypnotic Anesthesia for Major Surgical Procedure**
M. M. TINTEROW. *American Surgeon* [*Amer. Surg.*] **26**, 732–737, Nov., 1960. 23 refs.

After a brief review of the literature on hypnoanaesthesia the author describes the necessary preoperative training of the patient. Hypnosis is first discussed and any fears allayed. The patient is then conditioned and as deep a state of relaxation as possible is induced. Subsequently greater depth of hypnosis is secured and the whole operative procedure is gone through, the operative site tested for anaesthesia, and appropriate post-hypnotic suggestions given.

The advantages of hypnoanaesthesia are that it has no depressing physiological effects, it can be terminated instantaneously or continued indefinitely, and it is a pleasant experience free from any of the apprehension and tension so often associated with chemical anaesthesia. Further, there is no extra load on the circulatory, respiratory, hepatic, or renal system and no loss of reflexes during the operation; postoperatively, there is no pain at the operation site, no narcotics are needed, and the patient is able to move about freely. Hypnosis raises the pain threshold and apparently prevents the pain receptors in the higher cortical centres from being stimulated by noxious stimuli so that " the vegetative nervous system is able to maintain homeostasis and thus raise the adaptive response of the organism to stress ". Possible disadvantages of hypnosis are its over-enthusiastic use on patients not properly selected, the refractoriness of some subjects to hypnosis, uncertainty in producing the necessary degree of hypnosis, the time required, and public prejudice, while the application of the method by persons without adequate psychiatric training may be dangerous.

Seven cases are described in which operations were performed under hypnoanaesthesia only. In each case there were definite indications for using hypnoanaesthesia and all the patients were excellent subjects. An average of 5 to 6 sessions, each lasting about 30 minutes, were needed for preoperative training. The deep or somnambulistic state was produced, the technique being varied to suit the individual needs of the patient. The following operations were successfully performed: debridement of burns and skin grafting, vaginal hysterectomy, bilateral ligation and stripping of varicose veins, caesarean section, appendicectomy, haemorrhoidectomy, and open heart surgery for closure of an atrial septal defect.

F. E. Kenyon

1126. **Serial Cardiac Output Estimations during Anaesthesia with the Evans Blue Dye Dilution Technique.** [In English]
B. LÖF, I. R. VERNER, and J. P. PAYNE. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **4**, 91–96, 1960. 2 figs., 11 refs.

1127. **Effect of Suxamethonium on Cardiac Rhythm**
K. G. LUPPRIAN and H. C. CHURCHILL-DAVIDSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1774–1777, Dec. 17, 1960. 8 figs., 5 refs.

A slowing of the heart rate was found in 39 of a series of 41 patients after repeated suxamethonium injections. Electrocardiographic recordings showed this slowing was a sinus bradycardia in over two-thirds of the patients, with irregularities of rhythm occurring in the remainder. The nature of this arrhythmia was a depression of excitation and conduction of the cardiac impulse which in its severest form produced a cardiac arrest of seven seconds. The bradycardia or arrhythmia appears to be related to the size of the repeat dose used, and not to the number of doses or to the total amount of suxamethonium given.

Until further work has revealed the cause of these changes, atropine is suggested as a safeguard against these potentially dangerous effects.—[Authors' summary.]

1128. **The Determination of Cardiac Output during Anaesthesia**
J. P. PAYNE. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 422–431, Sept., 1960. 10 figs., 10 refs.

In the author's view the most valuable method of measuring cardiac output during anaesthesia is that provided by the dye dilution technique. He describes the technique used at Hammersmith Hospital, London, in which Coomassie blue is injected through a polyethylene catheter inserted into the superior vena cava. The ensuing arterial time–concentration curve is recorded by an ear oximeter. The method of calculating cardiac output is described and difficulties and disadvantages of the method are discussed.

This method has been used to determine cardiac output in patients undergoing anaesthesia with halothane. Induction of anaesthesia caused a slight rise in mean output which, however, was found not to be significant on statistical analysis. During the first hour of anaesthesia cardiac output rose gradually, but if anaesthesia was prolonged there was a tendency for the output to fall. After induction of anaesthesia with thiopentone in another group of patients there was also a slight rise in mean output, but maintenance with nitrous oxide and oxygen caused a gradual fall. *Mark Swerdlow*

1129. **Pediatric Anesthetic Experience in Using Tribromethanol for Cardiac Catheterization**
A. E. BLUNDELL, R. C. ANDRIELLO, and F. A. BALBONI. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 499–504, Nov.–Dec., 1960. 9 refs.

The authors describe their experience with tribromoethanol given rectally to 550 children undergoing cardiac catheterization at St. Francis Hospital, Roslyn, New York. A saline enema was given on the day before and on the morning of catheterization. Premedication in children aged 1 to 3 years was with codeine and atropine, while in children aged 4 years and over morphine and atropine were given. Half an hour before catheterization the child received per rectum 70 mg. of tribromoethanol per kg. body weight. Catheterization was carried out under local anaesthesia. The children generally slept throughout the procedure, and in all except 48 no anaesthetic supplement was necessary. In 15 cases the procedure lasted more than two hours and a further dose of tribromoethanol was required.
Mark Swerdlow

1130. **Clinical Evaluation and Observation of 14-Hydroxydihydromorphinone (Numorphan)**
J. C. APPLETON. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 505–510, Nov.–Dec., 1960. 6 figs., 3 refs.

In this paper from Miami Valley and the Good Samaritan Hospitals, Dayton, Ohio, the author describes the use of " numorphan " (14-hydroxydihydromorphinone) for premedication in 836 patients undergoing operation. The drug was given in a dosage of 0·75 to 1·5 mg. together with scopolamine and atropine; some of the patients also received quinalbarbitone, pentobarbitone, or promethazine hydrochloride. Numorphan was considered to produce adequate tranquillization without depression; there was little change in blood pressure and side-effects were minimal. The drug was thought to be particularly advantageous before spinal and before halothane anaesthesia and in the young and elderly. It was also given for the relief of postoperative pain in a dosage of 0·5 to 1·5 mg.; in children the dosage was 0·01 mg. per kg. body weight. In some cases the lack of sedative action detracted from the usefulness of the drug; the only serious disadvantage was a respiratory depressant effect.

[The inclusion of barbiturates and of promethazine hydrochloride reduces the value of this investigation.]
Mark Swerdlow

1131. **Alterations in Response to Somatic Pain Associated with Anaesthesia. III: The Effect of Hydroxydione**
J. W. DUNDEE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 450–452, Oct., 1960. 2 figs., 4 refs.

The author reports the results of studying the effect of hydroxydione on sensitivity to pain. The method of analgesimetry used was that previously described (*Brit. J. Anaesth.*, 1960, **32**, 396; *Abstr. Wld Med.*, 1961, **29**, 257), but the subjects of this study were undergoing major abdominal or thoracic procedures, it being considered that minor procedures did not justify the use of hydroxydione for induction of anaesthesia; 0·6 mg. of atropine was the sole premedication and no postoperative studies were attempted.

Hydroxydione was given to 10 patients in doses of 2 to 4 mg. per kg. body weight. In 9 of these cases there was no appreciable alteration in threshold or response readings up to 8 to 10 minutes after the injection, while in the 10th there was a definite decrease in sensitivity to pain. With larger doses, up to 16·4 mg. per kg. there was a definite decrease in sensitivity except in one case, in which 15 mg. per kg. produced a marked anti-analgesic effect. No rise in the response reading occurred until 3 to 5 minutes after the injection. The analgesic effect of hydroxydione was closely associated with its narcotic

effect. Further doses of hydroxydione given intermittently consistently increased the response readings, and the addition of 50% nitrous oxide in oxygen potentiated the analgesia.

These observations confirm those of Clutton-Brock (*Anaesthesia*, 1960, **15**, 71), who found no demonstrable anti-analgesic effect of hydroxydione, and accord with the general clinical experience of greater postoperative comfort when this drug is used for induction than when thiopentone is given. However, the author failed to detect any such difference when the dosage of thiopentone given before a major operation was only 200 to 300 mg. This accords with his previous postulation that the barbiturates exhibit an anti-analgesic effect only when the brain contains small or sub-anaesthetic concentrations, since with such a small preoperative dose virtually all the thiopentone would have disappeared from the brain before the end of the operation.

The author concludes that in its lack of anti-analgesic action hydroxydione possesses an advantage over thiopentone for the induction of anaesthesia and suggests that if other steroid anaesthetics possess this property it is to be hoped " that one can be synthesized with the same rapid onset of action as thiopentone ".

Michael Kerr

1132. **Alterations in Response to Somatic Pain Associated with Anaesthesia. IV: The Effect of Sub-anaesthetic Concentrations of Inhalation Agents**

J. W. DUNDEE and J. MOORE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 453–459, Oct., 1960. 6 figs., 25 refs.

In the last of this series of investigations the authors studied the effect on sensitivity to pain of certain anaesthetic agents given by inhalation in sub-anaesthetic concentrations. The effects of nitrous oxide, trichlorethylene, and diethyl ether were assessed in unpremedicated, fit medical students, whereas those of halothane were studied in patients undergoing minor operations to whom premedication with atropine was given. A non-rebreathing technique with high gas flows was used throughout, so that cyclopropane had to be excluded from the investigation owing to the explosion hazard. The graded pressure method of analgesimetry cited above [see Abstract 1131] was employed. After duplicate control readings had been taken inhalation was started and tests were made at intervals of one to 2 minutes for periods varying from 3 to 10 minutes. Threshold readings only were taken except in the case of halothane, when response readings were also recorded and the investigation was extended into the postoperative period, readings being taken at intervals of 5 to 10 minutes until they returned to the initial control level.

Inhalation of 50% nitrous oxide in oxygen rapidly raised the threshold reading, which reached its maximum in 2 to 4 minutes, there being no further increase on prolonging the administration; some degree of analgesia could be detected up to 2 minutes after withdrawal of the gas. Inhalation of 25% and 33% nitrous oxide in oxygen gave a maximum rise in 3 to 6 minutes. Trichlorethylene provided analgesia in concentrations of 0·35 and 0·5% in air, but in almost half the cases a transient increase in sensitivity to pain occurred at first; no unpleasant subjective sensations or restlessness accompanied this, however. Analgesia persisted longer after trichlorethylene than with any of the other agents studied. With 1 to 2% ethyl ether in air a definite analgesic effect was demonstrated; the onset was slower than with nitrous oxide and persisted up to 4 minutes after withdrawal. Even after 10 minutes' administration 0·5% halothane in oxygen failed to produce analgesia. Although the response reading was raised in the immediate postoperative period, it then fell below the control level, the duration of this anti-analgesic effect appearing to depend upon the duration of administration.

In discussing these results the authors offer some suggestions for clinical application and suggest that the use of 25 to 50% nitrous oxide in oxygen might be considered as a method of obtaining analgesia without loss of consciousness. The quicker onset of the analgesic effect of nitrous oxide and its lack of anti-analgesic effect makes it a better choice than trichlorethylene for use in obstetrics. Moreover, the " hangover " consistently experienced after trichlorethylene anaesthesia occurred after as little as 5 minutes' administration. Although ethyl ether showed analgesic properties, the irritation caused to the respiratory tract inevitably limits its value. The absence of pain relief with 0·5% halothane indicated that concentrations sufficiently high to produce analgesia are also likely to produce cerebral depression and hypotension, which thus renders this drug unsuitable as a sole agent for minor procedures; the shivering commonly encountered postoperatively may be explained by the increase in sensitivity demonstrated.

The authors consider that further study should be directed to finding out whether halothane is antagonistic to the analgesic effect of nitrous oxide or opiates. The effect of low concentrations of the azeotropic mixture of halothane and ether also merits investigation.

Michael Kerr

1133. **Trial of Two New Analgesic Agents**

M. SWERDLOW, J. L. MILLIGAN, and I. P. MCEWAN. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 553–556, Nov.–Dec., 1960. 2 refs.

Two new analgesics, RO4–0288 and RO4–1778, were tried as supplements to thiopentone–nitrous-oxide–oxygen anaesthesia at Salford Royal Hospital, Salford. After induction with 7 mg. of thiopentone per kg. body weight anaesthesia was maintained with nitrous oxide (6 litres a minute) and oxygen (2 litres a minute) in semi-open circuit. Doses of the analgesic were given as indicated by signs of lightening anaesthesia. The initial dose of RO4–0288 was 250 to 350 mg. and supplementary doses were 50 to 150 mg. The initial dose of RO4–1778 was 10 to 20 mg. and the supplementary doses were 2·5 to 10 mg.

It was found that RO4–0288 was a satisfactory adjuvant to anaesthesia but had no advantages over pethidine for this purpose. RO4–1778 was a less potent analgesic and was considered to be unsuitable for supplementation of anaesthesia.

Mark Swerdlow

Radiology

1134. **The Immediate and Long-term Results of X-ray Irradiation of the Tonsils and Pharyngeal Ring in Chronic Tonsillitis.** (Ближаишие и отдаленные результаты облучения рентгеновыми лучами миндалин и глоточного кольца при хроническом тонзиллите)
M. I. GLIKIN, O. S. IVANOVA, M. M. DUBOSARSKAJA, and L. A. MAJSTROVAJA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **38**, 127–128, Nov., 1960.

The authors report the results in 300 patients suffering from chronic tonsillitis who were treated with x-irradiation applied to the tonsils and pharynx through the skin. The x-ray tube was centred on the angle of the lower jaw; the field measured 6×8 cm., and other factors were 180 kV. with the usual filtration and 30 cm. focus distance, a dose of 100 r. being given at each treatment. The opposite side of the neck was irradiated with a similar dose on the following day. The whole treatment was repeated after one week. At the end of 4 years 45·5% of the patients were greatly improved and 44% moderately improved, while 10·5% derived no benefit from the treatment.
A. Orley

1135. **Electron-beam Therapy in the Management of Carcinoma of the Breast**
F. C. H. CHU, A. C. SCHEER, and J. GASPAR-LANDERO. *Radiology* [*Radiology*] **75**, 559–567, Oct., 1960. 13 figs., 2 refs.

Skin reaction or damage to underlying tissues often prevents the delivery of an adequate tumour dose by conventional radiation therapy in carcinoma of the breast. Recurrences in the chest wall and lymph-node metastases may thus develop in previously irradiated areas and the skin changes prevent further treatment by the usual techniques. In these circumstances high-energy electron-beam therapy appears to offer definite advantages. These are: (1) the electron beam has a sharp fall-off with penetration; (2) the depth of penetration can be regulated by varying the energy of the beam; (3) the maximum dose occurs at 10 to 15 mm. below the skin surface (at 22 MeV.); (4) irradiation is homogeneous; (5) there is little or no differential bone absorption; (6) the total volume of tissue irradiated is reduced, so that systemic reactions may also be expected to be reduced.

Between January, 1955, and December, 1958, 70 patients with cancer of the breast were treated with the betatron at the Memorial Center for Cancer and Allied Diseases, New York. Of these, 18 had inoperable disease, 14 were given postoperative irradiation after radical mastectomy or local excision, and 38 were treated for chest-wall recurrences or lymph-node metastases after surgery, irradiation, or both. The energy used was 22·5 MeV. Conventional fields were used, the dose given to the breast being 6,000 to 7,000 rads in 6 to 7 weeks and to the lymph-node fields 4,000 to 5,000 rads in 4 to 5 weeks. Metastases were treated with single fields. Of the 18 cases of inoperable carcinoma (of which 2 were of the inflammatory type), one failed to respond, in 10 the tumour completely disappeared, and in the rest it was reduced in size. The mean duration of regression was 11 months and the mean survival time 15 months. Skin reactions were minimal and 2 patients who had been treated with full doses at 1 MeV. 3 to 6 months previously tolerated the betatron irradiation without complications. Of the 38 cases of recurrence or metastasis, 5 failed to respond, but a favourable response was obtained in the remaining 33. The mean duration of response was 10 months.

It is concluded that the results obtained with electron-beam therapy in this class of patient are worth while and that the method offers advantages in the form of diminished reactions and fewer undesirable complications.
I. G. Williams

RADIODIAGNOSIS

1136. **Angiography of the Superior Sagittal and Transverse Sinuses**
L. MORRIS. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 606–613, Oct., 1960. 16 figs., 12 refs.

The superior sagittal sinus may be demonstrated by direct injection of contrast medium into the sinus via the fontanelle in children and after trephining in adults. This may be difficult or hazardous, however, and in this paper from Brook Hospital, London, a method is described whereby the superior sagittal sinus can be demonstrated by injection of the internal carotid artery. Radiographs to demonstrate the superior sagittal sinus are exposed 4 to 6 seconds after injection, the oblique half-axial view being the most satisfactory. For transverse sinus venography the radiograph is exposed 6 to 8 seconds after injection and both oblique positions may be necessary to show both transverse sinuses, although this may be achieved by a single radiograph in the straight half-axial view.

The superior sagittal sinus was demonstrated in almost 80% of cases when the internal carotid artery was injected, but in only 42% when injection was given into the common carotid artery. The normal appearances are described, those of the superior sagittal sinus not differing greatly from the textbook descriptions of its anatomy. The author states, however, that assessment of the transverse sinuses is not so straightforward, mainly because of anatomical variations. For instance, major dominance of one or other sinus was found in 4 of the 18 cases in this series in which the transverse sinuses were shown.

As regards the clinical application of the procedure, 6 cases are described in which sinography was of assistance in diagnosis or management, the conditions present in these cases being a meningioma (2 cases), sinus

thrombosis from a middle-ear infection (one case), and post-traumatic thrombosis (one case). In the remaining 2 cases traumatic thrombosis was suspected clinically but the sinograms were normal. Other conditions in which this method of investigation may be of value are discussed. *Arnold Appleby*

1137. **Combined Carotid–Vertebral Angiography—a Method of Vertebral Angiography: a Selective Procedure. Preliminary Report**
M. E. Berk. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 780–783, Dec., 1960. 7 figs., 10 refs.

In this paper from Johannesburg General Hospital, South Africa, the author describes his technique for visualizing the vertebral and carotid arterial systems simultaneously on the right side. The division of the right innominate artery into the subclavian and right common carotid arteries enables a catheter to be placed at the origin of both the right carotid and right subclavian systems, and therefore the right vertebral system.

The examination is carried out on the Lysholm skull table under local or general anaesthesia. A PE.205 Seldinger catheter is passed down the right common carotid artery as originally described by Seldinger in 1953 (*Acta radiol.* (*Stockh.*), **39**, 368). After much trial and error it was found that the optimum length of catheter to be inserted was 1 to 1½ inches (2·5 to 3·75 cm.); this ensured that the tip of the catheter was above the innominate artery. If the catheter was inserted further the contrast medium was forced into the thoracic aorta and rapidly diluted, resulting in poor visualization of the carotid and vertebral systems. A convenient total length of catheter is 15 inches (38 cm.). Haematoma formation can be alarming unless the artery is firmly compressed as the catheter is being removed and pressure at the site of puncture kept up for at least 5 minutes.

A disadvantage of the method is that only the right side can be visualized, but moderate success has been obtained in visualizing the left internal carotid system by compressing the left common carotid artery. [This could only be of limited localizing value in intracranial lesions.] A great advantage of the method is the simultaneous demonstration of the carotid bifurcation and the origin of the vertebral artery—both common sites of arteriosclerotic narrowing now amenable to surgery.
J. MacD. Holmes

1138. **Experimental and Clinical Tests with the High-pressure Injection Syringe of Gidlund in Selective Angiocardiography.** (Experimentelle und klinische Erfahrungen mit der Hochdruckinjektionsspritze nach Gidlund für die selektive Angiokardiographie)
H. Hallerbach and G. Luster. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortsch. Röntgenstr.*] **93**, 565–582, Nov., 1960. 14 figs., 4 refs.

The advantages of the Gidlund high-pressure syringe for the performance of selective angiocardiography are that the pressure is controllable and that air can be eliminated. The Gidlund syringe is actuated by compressed air, and in a series of experiments *in vitro* the authors have measured the rate of flow in a variety of catheters under varying pressures, using several different contrast agents in varying quantities. They have also used the syringe for angiocardiography in various heart conditions. They point out that there is a risk of damage to the heart wall due to incorrect position of the catheter during the injection, and contrast agent has been shown to escape into the pericardial sac. Nevertheless, they regard the Gidlund syringe as a valuable aid in performing selective angiocardiography. *F. M. Abeles*

1139. **Anthropological Factors Affecting the Estimation of Exposures Required for Chest Radiographs**
W. G. Clarke, S. M. Latham, and J. Thomas. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 695–700, Nov., 1960. 7 figs., 3 refs.

The antero-posterior chest diameters of 290 miners with varying degrees of pneumoconiosis and 280 non-miners were measured and plotted against the exposures as selected by the "iontomat" [an automatic exposure control] with the kilovoltage constant. The films were checked by a number of observers and were of acceptable quality. The results showed extremely poor correlation, for example, the exposures for the normal men with a 23-cm. chest diameter ranged from 24 to 40 mA., which suggested that the iontomat was compensating for a physical difference not directly related to the chest diameter. A number of other physical measurements were also made; from these measurements a nomogram was made: it was based on the antero-posterior diameter, weight and stem height. This was found to give a useful approximation of the correct exposures. This investigation suggests that ideally some form of automatic exposure control is necessary to produce consistently good quality chest films. In the absence of such control the use of a nomogram based on antero-posterior diameter, weight and stem height is suggested.—[From the authors' summary.]

1140. **Radiological Lung-function Studies**
R. E. Steiner, J. W. Laws, J. Gilbert, and M. J. McDonnell. *Lancet* [*Lancet*] **2**, 1051–1055, Nov. 12, 1960. 7 figs., 10 refs.

The authors, at the Postgraduate Medical School (Hammersmith Hospital), London, have devised a method of recording density changes in the lung with respiration and correlating this with a simultaneous recording of the movement of a spirometer. The apparatus for recording density consists of an image intensifier with a 5-inch (7·5-cm.) diameter field. The luminosity of the screen is translated into an electric current, which is amplified and made to drive a recording pen.

By visual means 2 areas in each lung were chosen for assessment—one just below the clavicle and the second a little way above the diaphragm. These zones could be selected visually before turning over to electrical recording. Changes in density that resulted from alterations in chest-wall thickness and movement of ribs were small and insignificant compared with the alteration in lung density resulting from respiration. Care was taken that

the diaphragm in its excursion did not impinge upon the field of observation. Vertically above the density recorder on the same drum was the recording pen of the spirometer in which the volume of the respired air was measured.

The authors found a close correlation between the movement of the spirometer needle and that of the densitometer. Imposed upon the curves of density variation were small waves which were attributed to alteration in lung density produced by the pulmonary vascular field; these were synchronous with the heart beats.

The findings in healthy subjects are illustrated, and 2 cases are reported where the tracings were not synchronous as a result, in one case, of bullous emphysema of the right lower zone and, in the other case, of an abnormal deficiency of pulmonary tissue on one side.

The clinical value of this radiological technique has yet to be assessed, and the authors hope to compare the findings obtained with those of more conventional lung function tests. *A. M. Rackow*

1141. **The Value of Pneumomediastinography in Primary Tuberculosis in Children.** (Значение пневмо-медиастинографии при первичном туберкулезе у детей)
A. Rusesku and M. Dzeormanjanu. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **35**, 14–16, Nov.–Dec., 1960. 12 figs.

In the investigation here reported pneumomediastinography was carried out on 100 children under treatment for primary tuberculosis at the First Paediatric Clinic, Bucharest. The authors used the direct transtracheal route and the quantity of air injected varied between 60 and 350 ml. according to the age of the child. The method, which produced no ill effects, enabled the exact location of the affected lymph nodes to be determined and the state of the mediastinal pleura to be assessed, and it also helped to exclude any lesion of the thymus gland which might be present. It proved particularly useful in cases in which surgical intervention was being considered for the treatment of primary tuberculous bronchoadenitis. *A. Orley*

1142. **The Diagnostic Value of Pulmonary Angiography in the Surgical Treatment of Lung Disease.** (Значение ангиопневмографии в диагностике некоторых хирургических заболеваний легких)
M. M. Voropaev. *Советская Медицина* [*Sovetsk. Med.*] **24**, 28–32, Oct., 1960. 3 figs., 15 refs.

After describing his method of performing pulmonary angiography the author discusses its diagnostic value with reference to 95 patients in whom the procedure was carried out for the purpose of differentiating inflammatory from neoplastic lesions of the lungs and mediastinum. By strict enforcement of all the necessary precautions side-effects were minimized. Films were exposed every second or half-second, this being sufficient to demonstrate the passage of the contrast medium all the way into the aorta. For the differentiation of different types of pulmonary disease alone 4 to 6 exposures taken at intervals of half a second were sufficient.

The angiopneumographic data obtained were compared with the bronchoscopic findings. A tumour is visualized as an avascular or poorly vascularized area, while the vessels round it are displaced, compressed, or obliterated, this being often associated with deformity or enlargement of the superior vena cava. The velocity of the circulation on the affected side is reduced, whereas on the opposite side it is increased and the vascular shadows exaggerated. In contrast to general angiopneumography, selective angiopneumography (for which only 10 to 15 ml. of the contrast medium is injected) brings into greater prominence the filling of the arteries, capillaries, and veins. It is stated that observation of filling of the capillaries gives the best indication of the condition of the lung segment being investigated. *S. W. Waydenfeld*

1143. **The Lower Esophageal Vestibular Complex. An Anatomic-Roentgen Study**
C. Zaino, M. H. Poppel, H. G. Jacobson, H. Lepow, and C. H. Osturk. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 1045–1055, Dec., 1960. 9 figs., 8 refs.

In 70 consecutive necropsies without regard to age, sex, race, or diagnosis the upper part of the stomach and the lower oesophagus with its diaphragmatic attachments were removed in one piece. In 51 cases the phreno-oesophageal membrane was carefully dissected and its division into upper and lower branches was " usually " found at the lower level of the hiatus, though occasionally it was displaced upwards. In 45 cases the insertion of the membrane into the longitudinal muscle of the oesophagus was studied microscopically. Its upper attachment was 1 to 4 cm. above the hiatus and its lower attachment was usually slightly below the hiatus. The vestibule of the oesophagus, 2 to 3 cm. in length, is defined as that segment of the oesophagus lying between the two attachments. On the inside its lower border was marked by the epithelial line at the junction of the gastric with the oesophageal mucosa; the upper border was marked by a number of prominent circular mucosal folds. The mucosa of the vestibule was usually different in colour from that of the rest of the oesophagus and it was more closely adherent to the underlying muscle. The muscle of the vestibular wall also differed from that of the rest of the oesophagus: the inner circular fibres were thicker and there were also spiral fibres and extra bundles just below the submucosa.

In 21 cases after removal at necropsy the specimen was attached to a special frame so designed that the diaphragmatic respiratory movements could be simulated. Metal clips were inserted at the oesophago-gastric epithelial junction, at the upper insertion of the phreno-oesophageal membrane, and at the lateral lips of the hiatus. Double-contrast x-ray films were then taken after distension of the specimen with air. A distinct saccular dilatation at the distal end of the oesophagus occurred. It was limited to the area between the upper and lower clips—that is, to the vestibule. No definite pinching of this dilatation by the oesophageal hiatus could be demonstrated. " Notching " at the level of the epithelial line occurred in 4 cases. The notches

corresponded to ridges of mucosa, and the ridges were produced by folds of muscularis mucosae.

The authors argue from these observations and from their experience with x-ray cinematography that the closing mechanism at the lower end of the oesophagus " is intrinsic in nature and located in the vestibule, which contracts and releases in its entirety ". The degree of the pinching action which occurs during inspiration depends on the pull of the phreno-oesophageal membrane, the reflex closing of the vestibule, or both.

[See also Abstract 1146. It is doubtful whether observations on necropsy material can sustain such an edifice of deduction.] *Denys Jennings*

1144. **A Classification of Esophageal Hiatus Hernia with Special Reference to Sliding Hernia**

G. HAGARTY. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 1056–1060, Dec., 1960. 5 figs., 28 refs.

The author analyses the radiological findings in 200 patients with hiatal hernia and classifies 86% as cases of " bell hernia ", 8% as cases of para-oesophageal hernia, and 6% as cases of massive hernia—that is, with almost the whole stomach in the chest. [The appearance of the " traction " hernia is not mentioned.] The author argues from the selected samples studied by surgeons [and in contradiction to the post-mortem evidence] that few herniae are completely reducible and that the appearance of a sliding hernia is an x-ray artefact.

[This is one of the few papers on hiatal hernia, in English, to give an accurate survey of the early literature.] *Denys Jennings*

1145. **Prolapse of the Mucosa at the Esophagogastric Junction**

A. A. DE LORIMIER and J. P. WARREN. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 1061–1069, Dec., 1960. 6 figs., 12 refs.

This paper gives a good review of the literature of oesophago-gastric and gastro-oesophageal mucosal prolapse and presents 4 case reports. In one of these cases there were no associated symptoms and in the others the complaints were variable. In the patient without symptoms the presence of prolapse led to a radiological suspicion of a neoplasm.

[Most of those with experience of the condition will probably be more doubtful than the present authors that prolapse is a cause of symptoms. The probability of its causing a misdiagnosis of carcinoma is quite high, especially if the patient is overweight and there is an associated hiatal hernia.] *Denys Jennings*

1146. **The Lower Esophagus**

W. S. KEYTING, G. M. BAKER, R. R. MCCARVER, and A. L. DAYWITT. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 1070–1075, Dec., 1960. 8 figs., 7 refs.

The purpose of this investigation was to study the lower oesophageal ring and its relationship to the oesophago-cardiac junction and hiatal hernia. Out of 1,131 consecutive radiological examinations of the upper gastro-intestinal tract a lower oesophageal ring was demonstrated in 12·8%. [A number of these rings are excellently illustrated.] Among 83 patients aged 20 to 29 years the proportion was 3·6%; in 236 patients aged 30 to 39 it was 8·5%; in 248 patients aged 40 to 49 it was 13·7%; and in higher age groups the proportion remained steady at about 15 to 16%. [The effect of sex and weight is not mentioned.] Among 100 control subjects without symptoms [not grouped according to age or sex] a ring was demonstrated in 14 cases. Only one patient with a ring could be studied at necropsy and in this case the ring, or the site of the ring, corresponded with the transition between the gastric and oesophageal mucosa. The authors " unreservedly support the concept that the ring is the cardio-oesophageal junction and that, therefore, when this ring is above the diaphragm, it indicates a hiatus hernia ".

[These authors' findings thus oppose those of Zaino *et al.* (see Abstract 1143). There is no discussion of the contradictory literature.] *Denys Jennings*

1147. **Roentgenologic Surveys for Gastric Neoplasms: Report of 31,895 Examinations**

R. S. SHERMAN and R. E. SNYDER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 949–956, Oct. 22, 1960. 7 figs., 16 refs.

The authors of this paper from the Memorial Hospital, New York, analyse the results of two surveys carried out to detect gastric neoplasms in asymptomatic patients. In the first survey fluoroscopy was carried out on 5,020 occasions, while in the second photofluorography was the method of examination in 26,875 instances.

In the first survey 11 tumours were found and confirmed; in one further case a tumour was suspected, but the findings at operation were negative. Of the 11 tumours, 3 proved to be malignant and were resected; all 3 patients are well, one of them up to 10 years after operation. The authors strictly applied the criterion that all patients examined must have been asymptomatic for at least one month; those with gastric symptoms of any kind were excluded and referred for a full gastro-intestinal examination.

In the photofluorographic survey 48 patients were found to have lesions either specific for, or probably suggestive of, neoplasm. Of these, 17 were operated on and the findings were: malignant growths in 4, adenomatous polyps in 8, ectopic pancreas in one, gastric leiomyoma in one, hypertrophic gastric mucosa in 2, and hypertrophic Brunner's glands in one. It is considered, on the basis of probability, that there were other malignant growths among those patients who did not submit to further investigation or surgery. The authors are more favourably impressed with fluoroscopy as a method of examination than photofluorography, largely because the close doctor–patient relationship which fluoroscopy permits is much more conducive to securing the cooperation of the patient in further examination and, if necessary, surgery. They consider that an efficiently organized screening session can be quicker than fluorography, which necessitates two independent readings.

Further, there need not be any significant radiation hazard if adequate precautions are taken.

The over-all findings are held to confirm the value of this type of mass survey, particularly in patients over the age of 45. *A. M. Rackow*

1148. **Radiological Investigation of the Small Intestine by Small Bowel Enema Technique**
F. PYGOTT, D. F. STREET, M. F. SHELLSHEAR, and C. J. RHODES. *Gut* [*Gut*] **1**, 366–370, Dec., 1960. 6 figs., 3 refs.

The Scott Harden technique of small-bowel intubation has been used successfully to examine 67 of 73 patients at the Central Middlesex Hospital, London. Of the remaining 6, one patient refused to cooperate before the examination began. The method was found to be particularly useful in revealing obstructing and infiltrating lesions. It is recommended that the procedure be confined to reasonably ambulant patients, who should have had a barium meal previously. The apparatus consists of 2 polythene tubes one inside the other, the outer one about 1 metre long and 4 mm. internal diameter, the inner one 1·5 metre long and 2·7 mm. outside diameter. The distal end of each tube can be identified on the image intensifier by a small brass ring bonded to it. Semi-rigid tubing should be used, but a short length of flexible tubing sheathed over the distal end of the outer tube is said to be an advantage.

Briefly, the procedure is to anaesthetize the pharynx and insert both tubes into the stomach with the outer tube leading slightly. When the greater curvature of the stomach is reached the patient is placed supine and, under screen control, the inner tube is advanced through the pylorus. If the inner tube tends to coil in the stomach the patient is rotated to the right and the outer tube advanced. Injection of barium is then made as required.
D. E. Fletcher

1149. **Transseptal Laevography.** (Die transseptale Lävographie)
L. STEINHART and J. ENDRYS. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortsch. Röntgenstr.*] **93**, 753–757, Dec., 1960. 4 figs., 21 refs.

From the Hospital of the Medical Faculty, Hradec, Czechoslovakia, the authors describe their method of performing selective transseptal cardiography of the left heart, which is an elaboration of the method of Ross *et al.* (*Circulation*, 1959, **20**, 793). A specially shaped catheter is introduced by the Seldinger technique into the femoral vein and after it has reached the right atrium the septum is perforated so that the tip of the catheter arrives in the left heart. The method has proved to be remarkably free of danger and at necropsy on a patient who died from other causes a clean puncture without thrombus formation was found in the septum. The method can be employed without general anaesthesia and without premedication, while one of its main advantages is that it permits of ordinary angiocardiography being undertaken, but if required the special kink in the catheter enables the cardiologist to continue with the selective filling of the left heart. It is claimed that this method is superior to all other methods proposed.
F. M. Abeles

1150. **Psoriatic Arthritis: a Roentgenologic Study**
R. AVILA, D. G. PUGH, C. H. SLOCUMB, and R. K. WINKELMANN. *Radiology* [*Radiology*] **75**, 691–702, Nov., 1960. 7 figs., 18 refs.

An investigation was carried out at the Mayo Clinic to determine whether psoriatic arthritis is a separate entity from rheumatoid arthritis. Radiographs of the hands, feet, and other joints of 155 patients with psoriasis and arthritic changes were compared with those of a control series of 100 patients with rheumatoid arthritis but without psoriasis. In the psoriatic group 31% showed lesions considered to be characteristic of the disease; in a further 31% such lesions were present in combination with others typical of rheumatoid arthritis, while in the remaining 38% the arthritic changes had a rheumatoid pattern. There was an increased incidence of rheumatoid arthritis in patients with psoriasis, this observation confirming the findings of other workers.

Radiological signs considered to be characteristic of psoriasis were: (1) destructive arthritis affecting predominantly the distal interphalangeal joints of the fingers and the interphalangeal joints of the toes, these joints being relatively rarely affected in rheumatoid arthritis; (2) bony ankylosis of these joints, a feature again rare at these sites in rheumatoid arthritis; (3) marked widening of the affected joint spaces with sharp demarcation of the eroded bony margins, a finding which is virtually pathognomonic; (4) bony proliferation round the base of the distal phalanx of the great toe with destructive arthritis of the interphalangeal joint, such changes being strongly diagnostic; and (5) resorption of distal phalangeal tufts. Radiological changes such as these were very rarely seen in the control cases. The features of osteoporosis and ulnar deviation of the fingers were much less common than in the rheumatoid group. In very advanced cases of psoriatic arthritis severe joint destruction of the " cup and pencil " type could closely resemble the late stages of rheumatoid arthritis. Nevertheless, on assembling all the radiological evidence, the authors conclude that a characteristic form of arthritis often accompanies psoriasis. *R. O. Murray*

1151. **Periureteral Fibrosis**
H. L. TWIGG JR. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 876–885, Nov., 1960. 5 figs., 27 refs..

In this paper from Georgetown University Medical Center, Washington, D.C., the author reviews 36 reported cases of peri-ureteral fibrosis and describes his experience in 4 additional cases. The ages of the 40 patients (31 male and 9 female) ranged from 23 to 75 years, average 43·7 years. In 33 cases the main complaint was pain in the back, flank, or abdomen, which sometimes resembled renal colic; only occasionally were there associated urinary symptoms, but vomiting and other gastro-intestinal disturbances were common. In most of the 23 cases in which the urine was analysed

erythrocytes or leucocytes were present. The blood urea level was raised in 20 of " 24 cases reported " and in most cases the haemoglobin level was reduced. Anuria occurred at some stage in about half the cases, while pyelonephritis was present in 18 cases and could not be excluded in a further 18.

Intravenous pyelograms showed hydronephrosis and hydro-ureter which tapered smoothly into a narrowed segment involving the middle third of the ureter, this last being sometimes displaced medially; the lower third of the ureter was of normal calibre. Sudden loss of function in a previously normal kidney occurred occasionally. In some instances obliteration of the psoas outline and occasionally an ill-defined soft tissue shadow in the loin were noted. Involvement was bilateral in 23 cases and unilateral in 17. On pathological examination the ureter was found to be surrounded by a mass of fibrous tissue containing scattered foci of chronic inflammatory cells. Ureterolysis and, if necessary, localized resection of the ureter and plastic repair with removal of the fibrous tissue were the most frequent operations. The author states that if the involvement is unilateral there is a " 25% chance [after surgery] that the other side will become involved within 3 to 12 months ".

Little information is available about the long-term prognosis, but early diagnosis is important if irreversible kidney damage is to be avoided. The aetiology is unknown, but it is suggested that the condition may possibly be an exaggerated local response to such stimuli as infection, tumour, or trauma. *Michael C. Winter*

1152. **The Radiological Assessment of the Mineral Content of Bone.** (Die quantitative Bestimmung des Mineralgehaltes der Knochen aus dem Röntgenbild)
F. Heuck and E. Schmidt. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortsch. Röntgenstr.*] **93**, 523–554, Nov., 1960. 25 figs., bibliography.

Writing from the Medical Clinic of the University of Kiel, the authors condemn all methods for the radiological assessment of the mineral content of bone which entail the use of step-wedges of aluminium, ivory, or bone. They have come to the conclusion that the material in bone that causes the radiographic shadow consists basically of calcium and phosphoric oxides roughly in the proportion of 3 to 1, and they find that the most suitable material for comparison consists of hydroxylapatite embedded in plastic. They use two step wedges with steps of 5 mm., one wedge containing 170 mg. of hydroxylapatite per ml. and the other containing 370 mg. per ml. The grain size of the hydroxylapatite is carefully chosen to resemble the size of the trabeculae of the normal bone. They first determine the thickness of the neck of the femur and of the os calcis. Both bones are then radiographed with the aid of equalizing water-baths or with equalizing plastic bodies, small areas of the radiograph being subjected to photometry in comparison with the calibrated step wedges.

Comparison of the results obtained by this method with those of chemical analysis of necropsy specimens of bone showed a maximum error of $\pm 10\%$. The method, it is claimed, makes allowance for all factors influencing film blackening such as processing, scatter of radiation, and variation in kilovoltage. *F. M. Abeles*

1153. **Angiography in Osteoid Osteoma.** [In English]
Å. Lindbom, N. Lindvall, G. Söderberg, and H. Spjut. *Acta radiologica* [*Acta radiol. (Stockh.)*] **54**, 327–333, Nov., 1960. 5 figs., 5 refs.

Jaffe's view that the osteoid osteoma is a peculiar kind of benign bone tumour is now generally accepted. Although the radiological appearance is commonly diagnostic, differentiation from sclerosing osteomyelitis or an intracortical bone abscess may be difficult. The authors of this report from the Institute of Radiopathology of Karolinska Sjukhuset, Stockholm, took advantage of the known hypervascularity of these tumours to investigate 2 cases by serial angiography. In each case contrast filling of the nidus took place, with in one case the demonstration of a small feeding artery, while in the other localized hypervascularity was revealed. Similar examination of 2 cases of sclerosing osteomyelitis showed no increased vascularity. One of these lesions clearly resembled an osteoid osteoma. The authors suggest angiography as a useful method for distinguishing between these entities. *R. O. Murray*

1154. **Percutaneous Transhepatic Cholangiography**
M. Atkinson, M. G. Happey, and F. G. Smiddy. *Gut* [*Gut*] **1**, 357–365, Dec., 1960. 8 figs., 28 refs.

According to these authors percutaneous transhepatic cholangiography is not so dangerous or unrewarding as previous authorities have considered. They carried out this investigation on 21 patients at St. James's Hospital, Leeds, using local anaesthesia and inserting a short-bevel needle (12 cm. long and 1 mm. bore) through the abdominal wall 2 to 4 cm. below and to the right of the xiphoid process. The needle was inclined in a slightly cephalad direction, and increased resistance was felt when it entered the liver. From this point onwards respiration was kept as shallow as possible to reduce the danger of laceration. A little saline solution was injected to clear the needle, and then constant suction was exerted by the syringe as the needle was inserted 6 to 8 cm. and then withdrawn.

It was not possible to enter the bile passages of 10 patients with intrahepatic obstruction, but in 11 cases of extrahepatic obstruction with dilated ducts the puncture was successful, though 2, 3, or even 4 punctures were occasionally necessary, inclining the needle in different directions to strike a duct. When a duct was entered, bile was aspirated; 10 to 20 ml. of 85% " hypaque " (sodium diatrizoate) was then injected and films taken. Such a concentration of contrast medium was found to mask calculi, so delayed films were also exposed as a routine.

Two patients had complications, one a biliary leak requiring laparotomy and the other abdominal pain and vomiting, which subsided. It must be borne in mind, however, that the procedure enabled an accurate diagnosis to be made in 11 cases of extrahepatic obstruction which would otherwise have required laparotomy for diagnosis. *D. E. Fletcher*